

# Ayurvedic and Allopathic Medicine and Mental Health

Proceedings of Indo-US workshop on Traditional Medicine and Mental Health  
(NIMH, Bethesda & NIMHANS, Bangalore)



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आ नो भद्राः क्रतवो यन्तु विश्वतः ।

*Aa no bhadraah kratavo yantu vishvatah*

*Let noble thoughts come to us from every side*

*- Rig Veda, I-89-i*

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# **Ayurvedic and Allopathic Medicine and Mental Health**

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Bharatiya Vidya Bhavan's  
Swami Prakashananda Ayurveda Research Centre  
(SPARC)

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**BHARATIYA VIDYA BHAVAN**

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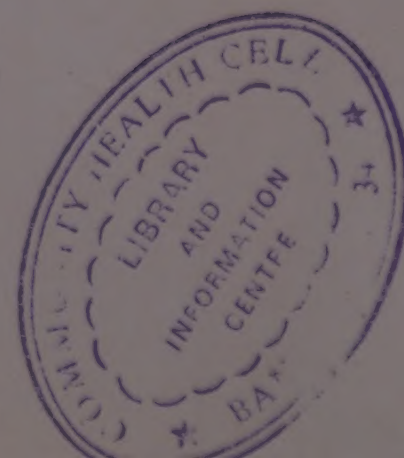
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## **DEDICATION**

To the memory of  
Two eminent participants  
at  
The Indo-US Workshop on  
Traditional Medicine and Mental Health  
Held at NIMHANS, Bangalore



**Dr. Krishnakant M. Parikh**



**Dr. George V. Coelho**





## General Editor's Preface

In 1977, a major project for a scientific correlation of Ancient Insights and Modern Discoveries (AIMD) was established by the Bhavan. The vision of the project was to bring together the experts, scholars and scientists for an interdisciplinary endeavour in (1) Science and Technology, (2) Life and Health Sciences and (3) the synthesis of Sciences and Human Values. Under the life and Health Sciences Division of the Bhavan's AIMD Project Swami Prakashananda Ayurveda Research Centre has carried out interesting AIMD correlation for research, service and education in Ayurveda and Life Sciences.

A team of vaidyas, physicians, super specialists and basic scientists have carried out short and long-term projects in hepatitis, diabetes, Parkinson's disease, cancer, women's infections, malaria, and arthritis. The work has globally enhanced the image of Ayurveda, as an evidence based health care system. Recently the senior scientists at Bhavan's SPARC, have been actively involved in the national and international research programmes, in Ayurveda. They were able to convince the Lord Walton subcommittee of the House of Lords of the British Parliament that Ayurveda has a robust base of professional, organozational and utilitarian activities. As a consequence, several countries are now giving an official status to Ayurveda in their health care.

In the Life and Health Science Division of the AIMD Project, publications / educational, scientific and practice-oriented were considered an essential activity. As a consequence, the **Bhavan's Book University** had the privilege of so far publishing the following books:

1. **Ayurveda and Modern Medicine** by Dr. R.D. Lele (1986),
2. **Selected Medicinal Plants of India** Chemexcil (1992),
3. **Holistic Living** by Prof. B. M. Hegde (1992),
4. **Safe Motherhood** by Dr. K. Bhaskar Rao (1995),
5. **Hypertension- Assorted Topics** by Prof. B.M. Hegde (1995),
6. **Gita and Health** by Vaidya Suresh Chaturvedi (1997),
7. **Herbal Cosmetics in Ancient India with a Treatise in Plants Cosmetics** by P.V. Bole & Kunda B.Patkar (1997),
8. **Culture, Philosophy and Mental Health** by Dr. A. Venkoba Rao (1997),
9. **High Blood Pressure** by Dr. Ashok B. Vaidya and Dr. Meenu Bhatt (1998),
10. **Guggul Ani Guggulkalp** by Vaidya Vasudha Vijay Apte (1998),
11. **Neem in Ayurveda** by Vaidya Suresh Chaturvedi (1998),
12. **Ayurveda for You** by Vaidya Suresh Chaturvedi (1998),
13. **Health is Wealth** by K. Balan (1999),
14. **In Search of Mind** by Dr. V. R. Deshpande and Ms. Sulbha Ghatate,
15. **Neem aur Ayurveda** (Hindi) by Vaidya Suresh Chaturvedi (2000),
16. **The Mind: Turbulent and Tranquil** by Dr. A. Venkoba Rao (2000),



17. **Ayurvedic Pharmacology and Therapeutic uses of Medicinal Plants** (Dhravyagunavignyan) Dr. Vaidya V. M. Gogte (2000)
18. **Garbhdaran: Nisanthan Honekeliye Marg Darshan** by Dr. Aniruddh Malpani and Dr. Anjali Malpani (2000),
19. **Kaayakalp** (Hindi) by Vaidya Suresh Chaturvedi (2002),
20. **Yoga Aur Sammohan-Ekatva Ki Raah** by Shri O. K. Shridharan (2002),
21. **Ayurvedic and Allopathic Medicine and Mental health** Edited by Vijayalakshmi Ravindranath, Linda Brady, Ashok D. B. Vaidya, George V. Coelho, Nityanand and Stephen H. Koslow (2002),
22. **Wisdom of the Human Body** by Prof. B. M. Hegde (2000)
23. **Hundred Years of happy and healthy life through Ayurveda and Yoga** (Jeevet Sharad Shatam) by Dr. S. P. Kinjawadekar (2002),
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25. **Who Am I ?** by Prof. Dr. B. M. Hegde (2002)

In the year 1998, a pioneering conference on Mental Health in Ayurveda and Allopathy was organized at Bangalore. The National Institute of Mental Health, Bethesda, USA and the National Institute of Mental Health and Neurosciences, Bangalore invited some of the best minds for a dialogue. The Bhavan, was approached by the organizers and the Zandu Foundation for Health Care, to publish the Proceedings of that symposium. The editors have done a remarkable job of creating a superb monograph. The Bhavan deems it an honour to publish the volume under its AIMD series of publications

It is appropriate that this volume is being dedicated to two pioneers, who had actively participated in the symposium but are no longer with us viz, Late Dr. Krishnakant M. Parikh of Zandu Pharmaceuticals and Dr. George E. Coelho of N.I.H. Their spirits will inspire the readership and we hope that this volume will provide a novel AIMD bridge for pragmatic services, advanced education and targeted research in the fields of psychiatry, Ayurveda and Neurosciences.

We hope this book **Ayurvedic and Allopathic Medicine and Mental Health** will be a worthy addition to our Ayurveda Sastra Series and will be warmly received by our esteemed readers in India and abroad.

**S. Ramakrishnan**  
General Editor  
**Bhavan's Book University**

*January 1, 2003,*



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# Ayurvedic Medicine, Its Approaches and Principles

R. H. Singh

Ayurveda is one of the most ancient medical sciences in the world. It is considered to be the Upaveda (part of) of Atharva Veda and thus has its origin from Vedas, the oldest recorded wisdom on the earth. It has survived through two sets of original authentic texts each consisting of three books, namely, *Vridhdhatrayi*, the three big books: *Charaka Samhita* (500 B.C.), *Sushruta Samhita* (500 B.C.), and the *Samhitas of Vagbhata* (600 A.D.); and *Laghutrayi*, the three small books: *Madhav Nidana* (900 A.D.), *Sarangdhara Samhita* (1300 A.D.), and *Bhava Prakasa* (1600 A.D.). All of these texts were originally written in Sanskrit and are in the form of an encyclopedia dealing with all aspects of life, health, disease, and treatment. The approach is essentially philosophic, holistic, and humanistic. Ayurveda is more life and health oriented than disease and treatment oriented. It presents a total life science and visualizes the total health of an individual in a holistic way.

Ayurveda advocates a complete restorative, preventive and curative system of medicine and appears to have been practiced in ancient times in the form of eight major specialties: *Kaya Cikitsa* (general medicine), *Salya Tantra* (surgery), *Salakya Tantra* (diseases of eye, ear, nose, and throat), *Kaumarabhritya* (pediatrics, obstetrics, and gynecology), *Rasayana Tantra* (nutrition, rejuvenation, and geriatrics), *Vajikarana* (sexology), *Bhuta Vidya* (psychiatry), and *Agada Tantra* (toxicology). Thus, Ayurveda was a well-developed system of medicine even in ancient times.

With the changing needs of the health care system today, the holistic approach of Ayurveda has once again drawn the attention of the world. There is a need to make full use of this ancient wisdom after due evaluation and scientific assessment to meet the newer

challenges of the medical world.

## The Approach

The extensive knowledge and wisdom about all aspects of medicine available in the Ayurvedic classics are very rich. Ayurveda, like all other systems of ancient Indian learning, made discoveries through the most subtle sources, namely, the *Pramana* (observations), *Pratyaksa* (direct perception), *Anu-mana* (logical inference), *Aptopadesa* (verbal and authentic documentary testimony), and *Yukti* (experimental evidence). In view of the above nature of the Ayurvedic knowledge, it is suggested that all studies and investigations directed toward its revival should take into account historical perspective, linguistic interpretation, and comparative evaluation of Ayurvedic medicine with contemporary sciences such as Western modern medical sciences.

If we examine the Ayurvedic concepts in the proper historical perspectives with the correct linguistic interpretations in the light of comparable contemporary knowledge, it may not be difficult to reach the genuine meaning. While undertaking the comparative studies, one has to appreciate that Ayurveda and contemporary modern medical sciences have very different approaches. The obvious distinctions between Ayurveda and Western medicine are: Ayurveda is essentially experiential, whereas modern medicine is an experimental science; Ayurveda has a holistic and totalistic approach whereas modern medicine is analytical; Ayurveda is function (physiological) oriented, whereas modern medicine is structure based and organ oriented. Ayurveda looks at the whole organism as a total indivisible being which



has to function as a whole in order to exist as a whole.

## **Fundamental Principles**

### **Microcosm-Macrocosm Continuum**

Ayurveda is based on the laws of nature. The theory of Loka-Purusa Samya (the macrocosm-microcosm continuum) is the most important principle; it states that the individual is a miniature replica of the universe. The individual and the universe both are essentially Panchabhautika (made up of five basic physical factors or elements). The elements are Akasa (ether or space), Vayu (air or motion), Teja (fire or radiant energy), Jala (water or cohesive factor), and Prithvi (earth or mass).

The Purusa (individual) and the Loka (universe) remain in constant interaction with each other and also derive and draw materials from each other in order to maintain normalcy and homeostasis. This exchange follows the law of Samanya and Visesa (homologous vs. heterologous) on the simple principle that similar/homologous matter increases itself, whereas dissimilar/heterologous matter decreases or depletes itself.

The interaction and exchange between Loka and Purusa continues in a natural way as an individual breaths air, drinks water, and consumes food articles available in nature. As long as this interaction is wholesome and optimal, the Individual is in optimal health. When a harmonious interaction breaks down, a disease state is initiated. Hence, the main principle of treatment of a disease is to restore harmony between the Loka and the Purusa and to restore the normal balance of Pancha Mahabhutas (five basic physical factors or elements) in the body and mind.

### **Ayu and Pancha Mahabhuta Theory**

Ayurveda conceives Ayu (life) as a four-dimensional entity consisting of Sarira (physical body), Indriya (senses), Satva (psyche), and Atma (the soul or the conscious element). Thus, the individual life being is a comprehensive psychophysical spiritual unit which is highly dynamic and is in constant interplay with the cosmos. The human body

is Panchabhautika, consisting of a proportionate combination of the five Mahabhutas (elements). The Pancha Mahabhuta Theory is essentially a theory of physics.

### **Theory of Tridosha**

The five Mahabhutas (physical attributes) constitute the Tridoshas- the three major biological components of the living body namely, Vata, Pitta and Kapha. The functions of the body are explained in terms of these Doshas. The biological components are called Doshas because of their inherent tendency to become vitiated and to vitiate each other. Vata is the biological product of the predominance of air and space, Pitta is the product of predominance of fire and water and Kapha is the product of earth and water factors of the Pancha Mahabhuta. Thus, the Tridosha theory of Ayurveda is a biological application of the Pancha Mahabhuta theory of Hindu physics.

The three Doshas can also be understood as conceptual constructs to explain human physiology in a unique holistic way. The human body consists of a mass of solid substratum with an intensive Interplay of chemical activity and an energy pool of motion and movement. These three aspects coexist in a predetermined proportion and function in a manner complementary to each other in the interest of the overall function of the total organism. The solid substratum of the body is called Kapha, the chemical moieties are the Pitta, and the energy or motion component is the Vata. The existence of the three Doshas can be felt in the body as a whole and can be traced at the molecular level.

Each cell of the body consists of a mass substratum, a chemistry, and an operative energy. They are the Kapha, Pitta, and Vata aspects of a cell's organelles, respectively. The proportion of the three has to remain in an appropriate range of normalcy which varies from organ to organ, tissue to tissue, and cell to cell. For example, a neuron in the brain may have higher degrees of Vata than the other two Doshas, while a cell of an endocrine gland such as the thyroid has more Pitta, and the relatively inert cells of the bone or muscle may have more Kapha.



## **Dosha Prakriti**

The relative proportion of the three Doshas (elements) is very important. The genetically determined relative proportion of the three Doshas within normal range is called Dosha Prakriti (personality). The properties of the Doshas are responsible for determining an individual's constitution, the sum total of his physique, physiology, and psyche. Thus, the Dosha Prakriti is an important consideration in understanding human life, health, disease, disease susceptibility, preventive and promotive health care, and treatment requirements of a patient. The Ayurvedic texts describe in detail the physical, physiological, and behavioral features of Individuals with different Prakritis. The texts describe seven types of Dosha Prakritis.

## **The Trigunas**

The Pancha Mahabhutas are represented in the psyche of an individual in terms of the Trigunas-the three Gunas (qualities) of the Manas (mind)-namely, Satva (clarity), Rajas (passion), and Tamas (inertia). Akasa Tattva (space) is represented in Satva Guna. Vayu (air) and Teja (fire) are represented in Rajas Guna. Prithvi (earth) and Jala (water) are represented in Tamas Guna. The Tamas Guna represents mass and inertia, whereas the Rajas Guna represents dynamicity and activity. Satva is the state of complete balance. The psychic makeup of an individual varies depending upon the genetically determined relative preponderance of the three Gunas. This variation is categorized as 3 major Manas Prakriti (mental constitutions) which are subdivided into 16 subtypes or traits. In principle, an individual's constitution reflects the combination of the 16 traits. However, one of the traits may predominate, giving characteristic features to the individual and defining the type of Manas Prakriti.

## **Swabhavoparamvada and Self-Healing**

Ayurveda propounds an important theory of self-healing termed Swabhavoparamvada (natural self-cure). According to Ayurveda, the human body is inherently endowed with a unique power of self-defense and spontaneous healing against injury and

disease. The body heals itself and a natural cure follows after every injury and insult. The role of medicine is to assist nature.

## **Basic Causes of Disease**

In spite of the rich resource of natural resistance and immunity of the body, technically termed Vyadhiksamatva, people do suffer from a variety of mental and physical disorders warranting medicinal interventions. Ayurveda propounds that the primary cause of all diseases is the failure of harmony between Purusa (the individual) and Loka (the universe or environment), an imbalance in the interaction of microcosm and macrocosm, respectively. Fundamentally, the Loka-Purusa interaction takes place at three levels: Kala (time and its chronobiological influences), Buddhi (intelligence, the major source of thought information), and Indriyartha (the objects of the five sense organs, the source of stressful information from the macrocosm to the microcosm).

The normal functions of Kala, Buddhi, and Indriyartha are important attributes of the life process. Their unwanted malfunctions are classically named Atiyoga (excessive utilization), Ayoga (nonutilization), and Mithyayoga (wrongful utilization). The Ayoga, Atiyoga, and Mithyayoga of Kala, Buddhi, and Indriyartha are named Kala Parinama (chronobiological changes occurring in the body as a result of alterations in time factors such as diurnal variations), Pragnaparadha (deliberate or volitional erring), and Asatmye-indriyartha Samyoga (unwholesome contact of sensory objects), respectively, and are considered to be the primary causes of all diseases. All other causes of ill health known and described in different schools of medicine are secondary to these primary factors, which are essentially environmental factors. Thus, the cause of disease according to Ayurveda lies in the environment, and so the cure is also to be found in nature.

## **Evolution of a Disease and Dosika Rhythm**

When an individual is indisposed because of the above-mentioned etiological factors, the disease process ensues in the form of Tridosika arrhythmia and vitiation of the



Doshas (physical elements), which may lead to irreversible diathesis and gives rise to a full-fledged disease. Sushruta Samhita, a leading Ayurvedic classic, describes six stages of the evolution of a disease, depicting each stage as a specific opportunity to apply appropriate therapeutic interventions. The Satkriyakala (stages of a disease) are Sancaya (accumulation of the Doshas), Prakopa (vitiation of the Doshas), Prasara (spread), Sthana Samsraya (localization), Vyakti (manifestation), and Bheda (chronicity and complications).

The precision adopted in describing these stages of the disease process and the relevant therapeutic intervention is a unique concept of Ayurveda. The basic philosophy behind the concept of Kriyakala (intervention time) is to emphasize the need for early detection of a disease and an appropriate timely therapeutic intervention so that the disease process may be reversed toward normalcy without waiting for later stages of the disease to become manifest. An Ayurvedic physician will detect the defect in the Sancaya stage, at the beginning stage of the disease.

### **Agni and Ama**

In the above context, it is often wondered why the Doshas start to accumulate. V-Ihat is the main triggering factor responsible for precipitating the Kriyakala (stages in the evolution of a disease)? Among many factors, Agni (the digestive and metabolic fire of the body) is considered to be the most important factor. There are 13 types of Agni in the body which are responsible for digestion of food and metabolism at different levels. When the Agni becomes weak, Ama (unwanted byproducts of digestion and metabolism) begins to accumulate in the body at different levels from the gastrointestinal tract to the systemic level in tissues and cells. Amas act as toxins and antigenic materials. Their presence renders an Ama state in the body which is characterized by increasing impermeability and sluggishness of the Srotas (body channels). The Ama state allows Sancaya (accumulation of the Doshas), the first Kriyakala leading to the progression of a disease. Ayurveda emphasizes that all diseases are the product of weak Agni (digestion and metabolism), and in turn the

main principle of treatment is to restore and strengthen the Agni.

### **Ayurvedic Diagnostics**

Diagnosis in Ayurvedic medicine is not always in terms of naming the disease, but is in the form of a description of the disease process depicting the pattern of vitiation of the Doshas (elements of the body) and Dusyas (seven basic tissues of the body) and the Adhithana (seat of origin of the disease), including the organs or Srotas (channels of the body) involved and the quality of life, health, and personality of the patient. All this demands a very extensive interrogation and examination of the patient. Ayurveda makes a twofold approach to diagnostics, namely, Rogi Pariksha (examination of the patient) and Roga Pariksha (examination of the disease pathology). Rogi Pariksha is essentially concerned with ascertaining the constitution of the individual and status of his health and vitality. It is not meant for the diagnosis of the disease.

The emphasis on ascertaining the constitutional background and evaluation of the status of health in a diseased person is a unique concept of Ayurveda. Ayurveda advocates that the patient is always of great help in making the diagnosis, in prognostication, and in deciding the overall approach in disease management and treatment.

Charaka, the foremost authority on Ayurveda, describes the Dasavidha Pariksha (a tenfold methodology used in Rogi Pariksha to assess the patient's health); it consists of Prakriti (constitution), Vikriti (current state of disease susceptibility or morbidity), Sara (quality of the tissues), samhanana (bodybuild or compactness of the body), Pramana (anthropometry, measurement), Satmya (adaptability), Satva (mental constitution or stamina), Ahara Sakti (digestive power), Vyayama Sakti (physical strength), and Vaya (age and rate of aging).

The Roga Pariksha (examination of the disease pathology) is carried out to diagnose the present state of the disease. This is usually done in three parts: Prasna Pariksha (the interrogation or patient history); Astavidha Pariksha (general examination by ne



the popular eightfold examination) including Nadi (pulse), Mutra (urine), Mala (stool), Jihwa (tongue), Sabda (voice), Sparsa (skin), Drk (eye), and Akriti (facial appearance or expression); and Sadanga Pariksha (systemic examination of the whole body including the Srotasas (13 gross channels) spread over the Sadangas (the 6 major parts of the body), namely, the head, neck, chest, abdomen, and the extremities. Nadi Pariksha (pulse reading) is considered to be one of the most important aspects of clinical examination. After acquiring the necessary experience and expertise, an Ayurvedic physician can determine a lot about the health and disease of the patient. Many physicians claim to depend entirely on pulse reading for making a diagnosis, although classical Ayurveda does not make such a claim.

### **Promotive and Preventive Health Care**

Ayurvedic Medicine is essentially promotive and preventive in its approach. However, it also provides a comprehensive system of curative medicine for the treatment of the sick, adopting a unique holistic approach. In accordance with the four-dimensional concept of Ayu (life), Ayurveda conceives a four-dimensional definition of Swasthya (health). Sushruta, one of the classic authors of Ayurveda, defines Swasthya as a state of Sama (balance) of the 3 Doshas, the 13 Agnis (digestive or metabolic factors), the 7 Dhatus (bodily tissue groups), and the Malas (impurities). A Swastha (healthy individual) is in a state of total biological equilibrium as well as Prasanna (a state of sensorial, mental, emotional, and spiritual well-being). Thus, Ayurveda presents a complete definition of health.

Ayurvedic texts describe a comprehensive regimen to maintain health, a code of health conduct popularly known as Swastha Vritta (daily and seasonal routines). This includes Dinacarya (the daily code of health conduct), Ratricarya (conduct for the night), and Ritucarya (conduct in relation to various seasons). Details about Sadvritta (codes) for lifestyle, diet, exercise, and personal and social hygiene have been described. Extensive information is available on

detail the role of periodic biological purificatory measures and consumption of Rasayanas (restorative remedies) for promotion of health, longevity, and Vyadhiksamatva (immunity or resistance against disease).

### **The Cure and Its Approach**

The object of curative treatment in Ayurveda is to restore the Dhatu Samya (balance of Doshas in the Dhatus-seven bodily tissues; equilibrium or homeostasis). The therapeutic attempt to restore balance is done by augmenting the weakened Doshas, decreasing the increased Doshas, and preserving the normal ones. Therapeutics consist of utilizing appropriate diets, drugs, and activities drawn from nature. Based on the principle of Samanya (homologous) and Visesa (heterologous), a similar or homologous material enriches the similar in the body and a dissimilar or heterologous material depletes its counterpart in the body. The concept of Samanya and Visesa is considered to be the fundamental basis of all actions in Ayurvedic treatment.

### **The Three Streams of Therapy**

Ayurveda describes three main types of therapeutic interventions which may be complementary to each other but are used more often to treat specific types of ailments. The three classical therapies are Daivavyapashraya Cikitsa (divine therapy), Yuktivyapashraya Cikitsa (biological, rational, or diet-drug therapy), and Satvavajaya (psychotherapy).

Daivavyapashraya Cikitsa is indicated in Karmik diseases (diseases caused by actions in past life), in cases where no definite acquired cause can be determined, and when Yuktivyapashraya Cikitsa is not effective. It is often practiced in tune with Astrology. Stars, stones, Mantra (chanting of hymns), Japa (chanting of sacred Incantations, meditation), oblations, prayers, and so on are the usual therapies for this purpose. This is a kind of Astrotherapy (spiritual healing). It is not psychotherapy or a therapy of biological significance.

Yuktivyapashraya Cikitsa is a rationally planned therapy taking into account the doc-



trines of Pancha Mahabhuta (five basic elements), Tridosha, Triguna, Agni, Ama, and so on and following the principle of Samanya and Visesa (homologous and heterologous). This is essentially a rational biological therapy aiming for Dhatu Samya (restoration of balance of homeostasis).

### Rational Ayurvedic Therapy

Rational Ayurvedic treatment is carried out in two parts: Samshodhana (purification therapy) and Samsamana (curative treatment). The aim of Samshodhana therapy, which is popularly known as Panchakarma therapy, is to purify the body from gross to subtle levels and to clean the Srotas (channels of the body) to enable the free flow of nutrients, medicaments, and metabolites. The living human body consists of innumerable Srotas which are traceable up to the level of the pores of cell membranes. The Srotas become blocked and sluggish as a result of age or ill health. Ayurveda advocates that these channels should be cleaned by Samshodhana measures in order to enable the individual to heal spontaneously and also to enable medicaments to reach the target sites more easily. Thus, Samshodhana is considered to be a prerequisite for all kinds of medications and therapeutic interventions.

A number of procedures are described for Samshodhana Karma. From a practical point of view, it is practiced in two forms, external or internal purification. External purification uses oleation, fomentation (hot compress which may contain herbs), and massage. A therapist uses oil baths, heat, and the physical pressure of massage as the tools of the treatment to soften and mobilize the Malas (impurities). External purification measures liquify the impurities and push them into gross channels (excretory systems) from where they are easily excreted or are expelled with the help of major internal purification procedures. Thus, external purification measures such as oleation, fomentation, and massage are considered to

be preparatory measures for the major internal purification therapies. Internal purification is the major intervention and consists of Vamana (emesis), Virecana (purgation), Anuvasana Vasti (oleus enema), Asthapana (nonoleus enema), and Sirovirecana (nasal instillations). The internal purification therapies are popularly known as Panchakarma (fivefold therapy).

In principle, Samshodhana Karma is followed by a specific Samsamana (curative treatment) that consists of a rationally planned diet, drugs, and lifestyle. In formulating a scheme of Samsamana treatment, the physician takes into account the patient's Prakriti (constitution) and components of his Vikriti (morbidity), namely the pattern of vitiation of the Doshas (physical elements), Dhatus (bodily tissue groups), Agni (digestion and metabolism), and so on. Ayurvedic physicians use the Panchabhautik composition of drugs and diets including their Rasa (taste), Guna (properties of the drug responsible for mediating its therapeutic actions), Virya (potency of pharmacological action), Vipaka (effect), and Prabhava (mechanism of action) and follow the law of Samanya and Visesa (homologous and heterologous).

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" To deal with the problems caused by technology, stress, artificial lifestyles and global pollution we are once again seeing the value of these natural healing systems .... which offer safe and proven remedies as an alternative..."

David Frawley



# Medicine : An Ayurvedic Understanding

N. S. Bhatt

Ayurveda represents one of the oldest known medical systems (2500 B.C.), the others being the Chinese, Tibetan, and Unani systems. These systems have a common approach in understanding the human biological process in relation to the universe. Each and every component of human life and the biosphere, including health and disease, can be co-related to external factors, the macrocosm. Because treatment aspects are based on principles which differ from those used in the present-day medical system, the totalistic or the holistic approach is reflected in the medicinal modalities as well.

It is difficult to understand the treatment principles in the language of present-day pharmacology. It may be possible to partially interpret the applications, but it is necessary to know the fundamentals of these systems to understand the principles underlying the biological activity of a process, drug, or therapy. In this chapter, the term medicine is used with its wider application, which includes all that is necessary to maintain health or treat a disorder.

This chapter tries to introduce a specific segment of an ancient medical knowledge base in an understandable language, but limitations of interpretation will make it necessary for the interested reader to delve further into details.

## What Is Medicine ? A Bheshaj (Therapeutic Approach)

Ayurveda recognizes 10 components of a medical system. These are the physician, therapeutics, disease or illness, treatment, longevity, the human body and relevant practice, periodicity, initiation of medical activity, and successful application of these activities.

The second and important component of medical treatment termed Bheshaj (a therapeutic) incorporates one and all therapeutic

approaches or therapies for the treatment of an ailment. Qualitatively these are of two types: Adravya (nonmaterial or metaphysical) and Dravya (material or physical).

Adravya includes a variety of therapies such as induction of fright, surprise, shock, pleasure, obliteration of memory, thrashing, binding, massage, or sedation. Dravya includes different kinds of therapeutic procedures as well as medicines.

Based on the therapeutic measures adopted, Bheshaj is further classified into two categories: Daivavyapashraya Cikitsa (divine therapy) such as rituals, chanting, wearing specific gemstones, sacrifice, devotional activities, and self-control measures, and Yuktivyapashraya Cikitsa (diet-drug therapy), which incorporates logical or experimental measures including other medicinal approaches.

## Pancha Mahabhuta Doctrine (The Theory of Five Elements)

The basis of the Ayurvedic philosophy is uniformity of the biological and physical world. Accordingly, the whole universe, including the human body, is composed of five Omni (substances or proelements named the five Mahabhutas): Akasa (space), Vayu (air), Teja (fire), Jala (water), and Prithvi (earth). Actually, these five represent the five subjects of the five sense organs, namely, sound of space, touch of air, vision of fire, taste of water, and smell of earth. The Mana (human mind) perceives the external world through five senses. This five-elemental Panchabhautik doctrine forms the basis of biophysical interactions. Table 1 lists the physical characteristics and attributes of the Mahabhutas.

The Mahabhutic doctrine also forms the basis of the effect of a therapeutic approach called the principle of Samanya and Visesa



(homologous vs. heterologous). In this approach, the harmonization between the biological entity and the material entity can be restored to normalcy by increasing or decreasing the causative factors. Accordingly, an excess of cold is balanced by heat, and anger is balanced by self-discipline. In lieu of a particular component, an increment of the related material will provide the balance.

All the substances according to the doctrine of Pancha Mahabhuta can be classified into five categories. Their properties and effects on the body are summarized in table 2.

### **Dravya Guna (Drug Action)**

"There does not exist anything in this universe that cannot be utilized as a medicine," says Charaka, meaning that all substances are potential therapeutics.

For such a broad derivation, understanding of the actions of a substance is vital. Any substance or entity that incorporates proper-

ties and effects (attributes and actions) is termed Dravya. The effects of a given Dravya (substance or drug) are based on its inherent properties. Therefore, in order to understand the pharmacodynamic aspects, knowledge about the Dravya Guna (pharmacological or therapeutic actions of a substance or drug) the Guna (pharmacological action), Rasa (taste), Virya (potency), Vipaka (effect), and Prabhava (resultant effect or mechanism of action) -is vital.

### **Guna (Action or Property)**

All Dravya (substances) are made of the five Mahabhutas (proelements) and exhibit properties based on the predominance of one or more of the inherent proelements. Guna is defined as the inherent inseparable property of a Dravya. There are 20 Gunas representing 10 pairs of opposite qualities or attributes of the composite ingredients of a given Dravya (table 3). These Gunas provide the basis for understanding physical and biological interactions.

**TABLE 1. - Mahabhutas: Physical characters and attributes**

Mahabhuta	Characteristics	Physical properties	Sense organ	Functions	Psychological property
Akasa (ether or space)	Sabda (sound)	Apratighat (nonresistant)	Srotra (ears)	distinction animation	Satva
Vayu (air)	Sparsa (touch)	Cala (movement)	Twak (skin)	sparseness lightness activity	Rajas
Teja (fire)	Rupa (vision)	Usnatva (heat)	Caksu (eyes)	color digestion sharpness brightness brevity	Satva
Jala (water)	Rasa (taste)	Dravatva (liquidity)	Rasana (tongue)	heaviness coldness oleation semen	Tamas
Prithvi (earth)	Gandha (smell)	Kharatva (roughness)	Ghrana (nose)	solidity heaviness	Tamas



**TABLE 2.** - Pancha Mahabhautika Dravyas (five properties of drugs or substances)

Group	Rasa (taste)	Properties	Effect
Parthiva (predominantly earth)	Madhura (sweet) slightly Kasaya (astringent)	Guru (heavy) Khara (rough) Kathina (hard) Manda (dull, slow) Sthira (stable) Visada (non-slimy) Sandra (viscous) Sthula (gross)	promotive for: growth weight compactness stability strength downward movement
Apya (predominantly water)	Madhura (sweet) slightly Kasaya (astringent) Amla (sour) Lavana (saline)	Sita (cold) Snigdha (unctuous) Manda (dull, slow) Guru (heavy) Sara (flowing) Drava (liquid) Mridu (soft) Picchila (slimy)	moistening oleation binding solvent pleasing
Taijasa (predominantly fire)	Katu (pungent) slightly Amla (sour) Lavana (saline)	Usna (hot) Tiksna (sharp, fast) Suksma (subtle) Ruksha (dry, not unctuous) Khara (rough) Laghu (light) Visada (nonslimy)	burning digestion luster complexion illumination tearing heating upward movement
Vayavya (predominantly air)	Kasaya (astringent) slightly Tikta (bitter)	Suksma (subtle) Khara (rough) Sita (cold) Laghu (light) Visada (nonslimy)	nonslimy lightness lassitude roughening movements
Akasiya (predominantly space)	Nonmanifest	Slaksna (smooth) Suksma (subtle) Mridu (soft) Visada (nonslimy) Vayavya (predominantly air)	softening porous lightness discriminate



Gunās, though inherent, are subjected to change due to any modifying process, termed Sanskar. For example, an otherwise toxic substance becomes a useful therapeutic after the Sanskar detoxification.

**TABLE 3.** - Guna: The 10 pairs of physical attributes of a Dravya (drug or substance).

Guru	heavy	Laghu	light
Manda	dull, slow	Tiksna	sharp, fast
Sita	cold	Usna	hot
Snigdha	unctuous	Ruksha	dry, not unctuous
Slaksna	smooth	Khara	rough
Sandra	viscous	Drava	liquid
Mridu	soft	Kathina	hard
Sthira	stable	Sara	flowing
Suksma	subtle	Sthula	gross
Visada	nonslimy	Picchila	slimy

These physical attributes inherent in the five elemental composition of a substance are manifested by its biophysical properties.

### **Rasa (Taste)**

Rasa in Sanskrit has many meanings, but in terms of pharmacological effect, it comprises six tastes perceived by the system through the tongue: Madhura (sweet), Amla (sour), Lavana (saline), Tikta (bitter), Katu (pungent), and Kasaya (astringent). The proportionate presence of the five proelements contributes to the formation of Rasa (taste). A Dravya may exhibit one Rasa such as Madhura (sweet) in the case of sugar or up to five Rasas in the case of fruits such as Haritaki, where all Rasa except Lavana (saline) are present. In addition to providing taste, Rasa impart specific physiological effects. Thus, the predominance of water and earth proelements of Madhura Rasa is useful for tissue building, whereas Katu Rasa with the predominance of fire and air will have more of a stimulant effect.

### **Virya (Potency)**

Virya is defined as the factor responsible for the action of a Dravya (drug or substance). It provides potency. All Dravya are classified into two categories: Usna (hot) and Sheeta (cold). Virya, consisting of two types, is responsible for the specific action of a Dravya. A Dravya in which Virya is compromised will lose its potency. The heat relation may indicate a stimulant or depressant effect of a substance.

### **Vipaka (Effect)**

The resultant effect of a Dravya (drug or substance) is termed Vipaka. Digestion and assimilation of a Dravya produce the Vipaka (transformation or effect) which is of three types—Madhura (sweet), Amla (sour), and Katu (pungent). In a way, this concept incorporates the kinetics of Dravyas as well. Madhura and Amla Rasas Dravyas produce a Madhura Vipaka; Amla Rasa produces an Amla Vipaka, and Tikta, Katu, and Kasaya Rasas produce a Katu Vipaka. The three resultant Vipakas provide three distinct effects on the body.

### **Prabhava (Comprehensive Effect or Mechanism of Action)**

Prabhava is defined as the final comprehensive effect of a Dravya. This effect can be dependent on the above-mentioned Rasa, Virya, and Vipaka factors, or independent of the same. It is the specific action of a Dravya. Of the factors, Virya (potency) is considered to be more effective than Rasa (taste) or Vipaka (effect). Prabhava explains the resultant effect. The process of metabolism is also important. It is mainly divided into two stages: Avasthapak (absorption at the initial gastrointestinal level) and Nishthapak (metabolic absorption at the tissue level).

The most important features of Dravya Guna (drug actions) in the Pancha Mahabhuta doctrine are the Gunas (attributes), which are expressed in terms of Rasa (taste), Virya (potency), Vipaka (effect), and Prabhava (comprehensive action), and are exhibited at different stages of digestion, metabolism, and the final biological effect. In short, every therapeutic effect can be explained in terms of Karma (action), Virya (potency), Adhikaran (site of action), Kala (duration), Upaya (mode), and Phal (the result).



### **Aushadhi Varga (Classification of Drugs)**

More than 1200 species of plants, nearly 110 minerals, including metals, and more than 100 animal products comprise the Ayurvedic pharmacopoeia. Substances are considered nutrients, medicines, or both. Plants, minerals, and animal products are described based on Rasa (taste), Virya (potency), Vipaka (effect), Prabhava (resultant action), and their nutritional or therapeutic effects. The therapeutic effects are classified according to causative factors, manifested conditions, or both.

Substances are generally classified based on the origin of the substance, the specific therapeutic action, those having more than one effect, and the treatment applications. Authors belonging to different periods have followed different methods of classification. Later books provide a comprehensive compilation of drugs under different categories. For the most part, groups of drugs are named based on similar therapeutic actions, effects, or after a representative substance.

*Charaka Samhita*, the most ancient Ayurvedic text, describes 50 groups of 10 plants each classified according to their therapeutic actions such as Jwaragna (antipyretics) or Mutral (diuretics) and specific applications such as Vamana (emesis) or Virecana (purgation). Sushruta, author of another treatise, describes 38 groups of plants with similar properties such as Ropan (wound healing), Shothagna (anti-inflammatory), Stanyajanan (galactagogue), or Arshogna (anti-hemorrhoidal).

These texts indicate knowledge about therapeutic actions or effects of different drugs or substances similar to present-day pharmacology. However, the terms Guna (properties), Rasa, Virya, Vipaka, and Prashava, which describe different actions or effects of a Aushadhi (drug), require proper clinical interpretation.

### **Aushadhi Karan (Pharmaceutics)**

The knowledge about pharmaceutics is well developed. Knowledge is available for the use of the juice of the fresh plant to that of powder, pills, infusions, medicinal oils, medicinal wines, and so forth as well as external application. Specific processes for e

detoxification of toxic substances and enhancement of the therapeutic actions are described in detail. In most cases, multiple composition and variety of the pharmaceutical process provides extensive flexibility to allow for the selection of a specific type of medicine or treatment.

In Ayurvedic literature, thousands of formulations are described with details of composition, quantity, process, general effect on humors, and specific clinical indications. Although plants are more commonly used as therapeutics, the use of metals such as gold, zinc, or copper and minerals such as mica or iron ores is not uncommon. Metals are processed specifically to ensure safety and to enhance their therapeutic effects.

### **Quality and Administration of Drugs**

Essentially, an ideal drug restores equilibrium or functional harmony. Any procedure which induces a therapeutic response is expected to not create any untoward side-effects. Due to its natural origin, a therapeutic should be available in abundance, rich in specific properties, have multiple uses, and be able to deliver the desired effect.

Safety and efficacy concepts are well defined. A drug or medicine is required to be examined in terms of its genesis, property, efficacy, seasonality, time of acquisition or procurement, preservation, and modification or process. Its application must be understood in terms of administration, dosage, patient compliance, and specific therapeutic effect. It is also necessary to understand its use in combination with other drugs and to compare it with other medicines with similar properties.

A medicine is considered appropriate if it can be given in small doses, has a rapid onset of action, and is easy to assimilate. It should be curative of a specific disease or increased morbidity and be safe even in complicated disease conditions. It should not have a depressant effect on metabolism, and it should be palatable, pleasing, and have good taste, odor, and color.

The time of administration of medicines is well specified, especially in relation to meals in the case of oral medicines. There are 10 different timings prescribed based on the



clinical indications: empty stomach (early morning), premeal, midmeal, postmeal, between two major meals (midday), with meals, and so on. The importance of time in relation to specific therapeutic effects is also mentioned. For example, medicines for anxiety disorders are prescribed at night.

### **Clinical Relevance**

More than 5,500 clinical signs and symptoms are available in Ayurvedic texts. The diseases are classified based on the Tridosha and Pancha Mahabhuta doctrines or humoral theories. The three Doshas (humors) - Vata (wind), Pitta (bile), and Kapha (phlegm)-represent Akasa and Vayu (space and air), Teja and Jala (fire and water), and Teja, Jala, and Prithvi (fire, water, and earth) presubstances, respectively. Several groups of diseases are described with subgroups. For example, there are 108 different conditions leading to Jwara (fever), and 20 different types of dysuria, including one which resembles diabetes. The medicines can be

used singly, in combination, or in the form of therapies with specificity. It is beyond the purview of this chapter to provide a comprehensive and full understanding of clinical application of Ayurvedic therapeutics.

### **Conclusion**

Ayurveda is one of the most ancient systems of medicine. It is of Indian origin and has much to offer in terms of therapeutics of natural origins. Ayurveda provides a systematic knowledge base of nutrients and drugs which can provide potential candidates in the search for novel therapeutics and can positively contribute to existing medical knowledge. There are definite possibilities to co-relate clinical manifestations and biological happenings based on a logical understanding. Specific therapeutics and treatments prescribed for different diseases may provide leads for the treatment of conditions that are difficult to cure.

There are about 121 prescription drugs, in modern medicine, that are derived from higher plants. The use of plants in traditional medicine has been a rich source for modern therapeutics.... Norman Farnsworth has estimated that only 5000 plant species have been investigated significantly out of the estimated total of 250,000 to 300,000 species...

Therapeutic wisdom of a culture is a dynamic experience base that demands close participation for understanding and learning. The approaches to such a wisdom are often conditioned by the dominant ethos of other cultures or individuals. One approach can be scholarly study in an anthropological sense. The other dominant approach can be scientific investigation of therapeutic practices and the pragmatic utilization of demonstrated therapeutic wisdom.

*-T. R. Govindachari*



# Perspective on Ayurveda With Special Reference to Mental Health

D. S. Antarkar

The earliest reference to medical science is seen in Atharva Veda, written about five thousand years ago. However, a systematic and detailed description is given in *Sushruta Samhita*, *Charaka Samhita*, and *Ashtang Sangrah*. These texts were written between 2500 and 600 B.C.

Sushruta describes the method for dissection of the human dead body. Six layers of the skin are identified. The fourth layer of the skin is named Tamra (containing copper). Leukoderma (vitiligo) has been mentioned as the disease of the fourth layer. Surprisingly, copper is also being used as the therapeutic agent in the treatment of leukoderma.

Various systems such as Prana vaha srota (respiratory tract), Anna vaha srota (gastro-intestinal tract), and Mutra vaha srota (urinary tract) have been described. Normal functions, signs, and symptoms of pathological conditions of these systems have been explained.

Pathological functions and symptoms of pathophysiological conditions are described in terms of normal and abnormal functions of the Tridoshas-Vata, Pitta and Kapha- and of the Dhatus (the seven bodily tissue groups) - Rasa (plasma and lymph), Rakta (blood), Mamsa (muscle), Meda (adipose), Asthi (bones and cartilage), Majja (marrow and nerve tissue), and Shukra (male reproductive tissues).

The eight major sections of Ayurveda are Kaya Cikitsa (general medicine), Bala Cikitsa (pediatrics), Graha Cikitsa (spiritual therapy, not mentioned in today's medicine), Urdh-wang Cikitsa (ear, nose, throat, and eye), Salya Cikitsa (surgery), Jara Cikitsa (geriatrics), Danshtra (toxicology), and Vrushya Cikitsa (endocrinology and the reproductive system).

The structure and function of the organs have been well recorded. The heart has been described as a muscular organ which pumps blood into the circulatory system through

Dhamani (arteries) and receives blood back from the body by the Sira (veins). The gastrointestinal tract consists of the Amashaya (stomach), which receives food and secretes Pitta (acid) and Kapha (mucus). The Pitta digests food and the Kapha protects the mucous membranes of the gastrointestinal tract.

## Disease Classification

Diseases have been classified according to their presumed causative factors: Adibala Pravritta (genetic), Janmabala Pravritta (congenital), Doshabala Pravritta (functional, caused by vitiation of one or more of the three Doshas), Sanghatbala Pravritta (traumatic), Kalabala Pravritta (seasonal), Daivabala Pravritta (providential), and Swabhavabala Pravritta (natural or inherent).

Diseases are described in terms of Nidana (etiology), Purvroopa (prodromal symptoms), Rupa (signs and symptoms), Samprapti (pathogenesis), Sadhyasadyatva (prognosis), and Cikitsa (therapeutics).

Therapeutics consist of Langhan, Brinhan, and Rasayana. Langhan is of two types: Shodhana, and Samsamana. Shodhana includes emesis induced by therapeutic agents; enemas induced by rectal use of decoctions of plants, medicated oils, and other agents used specifically for a particular disease; purgatives; the use of drugs through the nose; and blood letting. Shodhana is a cleaning process in which vitiated substances are eliminated. This mode of treatment is also known as Panchakarma (five types of procedures). Samsamana treatment includes use of drugs through the oral route as well as nondrug therapeutics such as fasting.

Drugs are from three sources: plants, animals, and inorganic substances. Various parts of the plants such as roots, stem, leaves, and seeds are used. The most commonly used plant preparations are fresh juice,



powder of the dried part, decoctions prepared out of the plant parts, dried water extracts, and self-generated wines.

Some of the most popular preparations are Bhasmas (herbomineral preparations) of various minerals such as mica, copper, and zinc. The minerals are treated with plant juices and heated. The process is repeated many times. Such herbomineral preparations are very commonly used today in Ayurvedic clinical practice.

Diseases have also been classified simply as either physical or mental, although physical and mental symptoms can be present in either type.

*Sushruta Samhita* describes the features of the mental diseases as Harsha (elation), Krodha (anger), Shoka (sadness), Bhaya (fear), Dainya (misery), Vishada (depression), Kama (sexuality), Ersha (jealousy), Lobha (greed), Asuya (fault finding), and Matsarya (hatred).

Elation, sadness, misery, sexuality and greed are due to overdesire, whereas anger, fear, depression, jealousy, and fault finding are due to hatred. These features are part of a normal life. The features are considered to be pathological when they disturb the normal life of a person.

Physical functions are controlled primarily by the three Sarira doshas, Vata (wind), Pitta (bile) and Kapha (phlegm), whereas the mental functions depend upon the three Mano doshas, Satva (clarity), Rajas (passion), and Tamas (inertia, lethargy). The separation of functions, however, is not exclusive. Vata can also initiate and control mental functions. Normal functioning of Vata induces delightfulness and liveliness. Abnormal functioning induces confusion, fear, sadness, misery, excessive talk, and insomnia. A person with normal functioning of Pitta is brave, intelligent and short tempered. Abnormal functioning of Pitta induces fear.

Normal functioning of Kapha initiates good sexual function, alertness, and enthusiasm; the individual is knowledgeable, intelligent, and tolerant. Sexual debility, laziness, idleness, and confusion are induced by abnormal functioning of Kapha. Thus, there seems to be a close link between Vata, Pitta, and Kapha, which mainly control the physical functions and functioning of the mind, which is controlled primarily by Satva, Rajas, and

Tamas.

There are various examples where abnormal functioning of the mind is shown to be responsible for physical disease. Charaka Samhita mentions that abnormal functioning of the mind is responsible for cardiac pain, and this has been substantiated by objective evidence in well-designed controlled studies carried out at a hospital specialized in cardiac care in Montreal.<sup>1 2</sup> Sixteen percent of the sample of postmyocardial infarction patients with major depression subsequently showed fivefold higher mortality which was independent of their underlying cardiac status.

Pharmacological approaches are being considered to be potential interventions for psychological factors in coronary heart disease. Selective serotonin reuptake inhibitors (SSRIs) are not only effective as antidepressants with a favorable side-effect profile but also have effects that may reduce risk of coronary heart disease directly. These agents have the potential to decrease sympathetic nervous system activation, deplete platelet serotonin stores, and decrease anger and aggression. Surprisingly, some Ayurvedic formulations used for coronary heart disease are also useful for depression.

A number of factors have been found to be responsible for good mental health. Happiness is quite important. There are mood swings in everyone's life which are determined by outside reality. However, people return to their usual level of happiness without any intervention. Studies carried out in several countries have found that money does not co-relate with the perception of happiness except among the very poor. Education, marriage, and family have not been found to correlate with happiness. Each factor may make a person a little happier but has minimum impact in comparison to an individual's characteristic sense of well-being. In a study of 1,500 pairs of identical and nonidentical twins, it was estimated that half of a person's sense of well-being was due to an inherited set point. This supports the view of Ayurveda that an individual's mental constitution is only partially due to the genetic background and that intervention is possible to the extent that the mental constitution is not genetically decided.



Unmada Gajakesari is a formulation of choice for the treatment of Unmada (psychosis). The formulation contains one part of processed mercury, one part of processed sulphur, one part of processed Mansheela and three parts of processed seeds of *Datura alba*. The mixture of these ingredients is processed seven times with fresh juice of *Centella asiatica* and a decoction of the plant *Acorus calamus*. Both of these plants as well as Mansheela are useful in mental diseases.

Smritisagar Rasa contains one part of processed mercury, one part of processed sulphur, one part of Tamra Bhasma, one part of Mansheela, and one part of Hartal. The mixture is processed with the fresh juice of *Centella asiatica* 21 times and once with the oil of *Celastrus paniculatus*. This formulation is commonly used for epilepsy.

Laxmivilas Rasa (Naradeeya) contains 15 ingredients including Abhraka Bhasma. This is the most commonly used formulation for depression and needs to be Investigated with priority.

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#### C.N.S - Active Ayurvedic Plants Medicinal Plants

- |                           |                             |
|---------------------------|-----------------------------|
| (1) Aegle marmelos        | (9) Evolvulus alsinoides    |
| (2) Allium sativum        | (10) Ferula foetida         |
| (3) Asparagus racemosus   | (11) Ficus religiosa        |
| (4) Butea frondosa        | (12) Mucuna pruriens        |
| (5) Celastrus paniculatus | (13) Nardostachys jatamansi |
| (6) Centella asiatica     | (14) Terminalia belerica    |
| (7) Crocus sativus        | (15) Withania somnifera     |
| (8) Eclipta alba          | (16) Zingiber officinale    |



# Development of new Centrally Acting Drugs From Ayurveda

B. N. Dhawan

Mahler,<sup>1</sup> the then Director General of the World Health Organization (WHO), made the following statement in 1977.

"For too long, traditional systems of medicine and 'modern' medicine have gone their separate ways in mutual antipathy. Yet, are not their goals identical-to improve the health of mankind and thereby the quality of life? Only the blinkered mind would assume that each has nothing to learn from the other".

Unfortunately, the situation has not changed much, and only in recent years has there been a resurgence of interest in the exploration of drugs used in traditional systems of medicine to develop new drugs.

Ayurveda is one of the best developed systems of traditional medicine. It has been described as an eternal omniscient system of medical science which promotes universal good and is worth a lifetime of study.<sup>2</sup> The major classes of centrally acting drugs have originated from plant sources. A recent example is the neuroleptics which were discovered as a result of clinical and experimental revaluation of the Ayurvedic drug *Rauwolfia serpentina* using modern procedures. Another important new molecule is coleonol,<sup>3 4</sup> also known as forskolin,<sup>5</sup> a potent activator of adenylate cyclase.<sup>6</sup>

## Ayurveda Versus Modern Concepts

There are, however, several difficulties in developing Ayurvedic drugs suitable for use in modern medicine. Ayurveda has a holistic concept, not only in terms of treating the human body as a whole, but also in using plant materials with minimal fractionation. Very often several plants are used together for synergistic activity. Modern medicine follows

a reductionist approach that emphasizes the use of pure simple compounds. This leads not only to wastage of plant material and use

of complex technology but very often also to reduced therapeutic activity.

It is necessary to have a composite team of experts in Ayurveda and modern medicine in order to understand the Ayurvedic system properly and to identify and select suitable Ayurvedic remedies for development as modern drugs. A thorough knowledge of Ayurvedic concepts is helpful in translating them to modern concepts and may facilitate the development of investigational drugs based on Ayurvedic preparations. Satyavati<sup>7</sup> first showed the close correlation between the Ayurvedic and present day concepts of hyperlipidemia. Similar studies in the central nervous system (CNS) should also be fruitful. Table I compares the manifestations of Kapha Prakriti in Ayurveda with the effects of muscarinic stimulation. The information in table 1 is based on studies of Raju<sup>8</sup> and shows a remarkable similarity in most of the organ systems.

## The Approaches

Many plants used in Ayurveda for the treatment of CNS disorders have been investigated in Indian laboratories, but systematic studies have been done on very few of these plants. The most commonly employed procedure is to prepare extracts of selected plants (e.g., in alcohol) and to subject them to appropriate animal tests. A second and less commonly used method is to conduct clinical studies using Ayurvedic preparations. The third approach is to subject the plants to a broadbased biological screen irrespective of available data on its clinical use in Ayurveda. In many of these studies, proper botanical authentication of the plant has not been done, and information on the time or place of plant collection is not available.

In our studies, plants were collected and authenticated by experienced botanists, and



**TABLE 1.** -Similarities between the manifestations of Kapha Prakriti and muscarinic stimulation.

Kapha Prakriti	Muscarinic Stimulation
Central nervous system	
1. Divaswapnam	hallucinations
2. Alasyam	rest, sleep
3. Budhim	learning
4. Gnanamagnanam	memory
Gastrointestinal tract	
1. Mukha Sravascha	salivary hypersecretion
2. Avipakti	increased peristalsis
3. Malyasyadhikam	excessive purging
4. Triptisha	nausea
Cardiovascular system	
1. Hridayopalepa	bradycardia
2. Dhamni Chayascha	vasodilation
Respiratory system	
1. Kanthopalepa Bandha	bronchoconstriction
2. Shelshmoda Gharnacha	bronchial hypersecretion
Others	
1. Styimiyam Shetangiche	sweating
2. Swatamutracha	involuntary micturition
Bahumutracha	frequent micturition

herbarium specimens were preserved in each case. The results of these studies have been periodically reviewed.<sup>9-13</sup> Selected agents are discussed here.

### Animal Studies

The Ayurvedic classification of CNS drugs includes about 10 classes of products, including analgesics, antipyretics, hypnotics, antiinsanity (neuroleptics), and memory enhancers. Most of these products have not been properly investigated using modern procedures. Even in the case of Ayurvedic plants that have been well characterized, limited animal studies have been done. The majority of animal studies have been done using crude extracts of Ayurvedic plants with no attempt to isolate and characterize the active constituents. Lists of such plants have been provided in several reviews.<sup>10 12 15</sup> In some cases, active constituents have been

isolated. These findings have been reported in a previous review.<sup>13</sup> Detailed pharmacological studies have on been done in a few cases, and in only one case, a preclinical and safety evaluation has been followed by clinical studies.

*Acorus calamus.* - The roots and rhizomes are used in Ayurvedic preparations. The active principles were isolated by Baxter et al.<sup>16</sup> and characterized to be an  $\alpha$  and  $\beta$  asarone. Asarone exhibits marked CNS depressant activity in a variety of laboratory animals.<sup>17</sup> The effects resemble those of reserpine and chlorpromazine, although the levels of catecholamines and 5-HT are not altered. Detailed structure activity studies have been performed on semi synthetic derivatives of asarone, but no better compound has been developed.<sup>18</sup> A preliminary clinical trial has not yielded very satisfactory results,<sup>9</sup> and no further studies are planned.

*Nardostachys jatamansi.* - A sesquiterpene, jatamansone, has been isolated from the essential oil present in the root stock. It has potent tranquilizing activity and a good therapeutic index.<sup>20 21</sup> The oil itself also has anticonvulsant activity.<sup>22</sup> Some clinical studies have been performed with jatamansone,<sup>21</sup> but there has been no followup. The results provide a rationale for extensive use of the plant in Ayurvedic practice.

Many plants are used in Ayurveda as Medhya (to promote intellect and memory). The main plants are listed in table 2. Clinical studies with five of these plants are discussed above or in the next section.

*Bacopa monniera.* - The two drugs which are used frequently and are classically advocated for the treatment of psychological and psychosomatic disorders are *Bacopa monniera* and *Centella asiatica*. Both are referred to as Brahmi, although *Centella asiatica* is generally called Mandukaparni. Of these two, *Bacopa monniera* is more potent according to most Ayurvedic texts, whereas *Centella asiatica* is used more often as a vegetable in dietary regimens.<sup>22</sup> We, therefore, decided to undertake indepth studies on *Bacopa monniera*.

Our initial studies were performed with a 90 percent ethanol extract of *Bacopa*



**TABLE 2.** -Plants commonly used in Ayurveda as Medhya.

Botanical name	Part used
<i>Acorus calamus</i>	rhizome
<i>Bacopa monniera</i>	plant
<i>Benincasa hispida</i>	seed oil
<i>Celastrus panniculatus</i>	seed oil
<i>Cèntella asiatica</i>	plant
<i>Convolvulus pleuricalis</i>	plant
<i>Emblica officinalis</i>	fruit
<i>Nardostachys jatamansi</i>	root
<i>Terminalia chebula</i>	fruit
<i>Tinospora cardifolia</i>	stem

*monniera*. Its effects on acquisition, consolidation, and retention were tested in albino rats using the conventional Y-maze and conditioned avoidance and Sidman's avoidance procedures. The results in all of the tests indicated that the extract facilitated cognitive function and augmented retention.<sup>23</sup>

The next logical step was to isolate and characterize the active constituents. A number of saponins were isolated from the plant, the main ones being bacosides A<sup>24</sup> and B.<sup>25</sup> Bacoside A has since been shown to be a composite of several saponins.<sup>26</sup> The chemical structures of bacosides A<sub>2</sub> and A<sub>3</sub> have been established and are shown in figure 1. Bacoside A<sub>1</sub> is a minor constituent of *Bacopa monniera*.<sup>27</sup> The chemical structure of Bacoside B may need to be revised. The mixture of saponins is as effective as the individual saponins and is obtained more easily and in much greater yield. Therefore, we used the mixture of saponins isolated from the plant in the Y-maze, conditioned avoidance, and Sidman's avoidance test systems. The same effects were obtained as with the crude extract, only with much lower doses.<sup>28</sup>

The mixture of saponins was further tested in the conditioned taste aversion model of Brozek et al.<sup>28</sup> In this test, a facilitory effect on cognitive function and retention was also obtained at low doses.<sup>29</sup> Bacosides also reversed amnesia induced by immobilization, electroconvulsive shock, or hyoscine.<sup>30</sup> They

have also been shown to have potent antioxidant activity.<sup>31</sup> Bacosides have been found to be safe in subacute toxicity studies in rats and rhesus monkeys, and in Phase I clinical studies in normal human volunteers using single doses or repeated doses for 4 weeks. Phase II clinical studies are being initiated. It also has been possible to standardize a traditionally used extract by regulating its bacoside content, and the product is being marketed as "Memory Plus" capsules.

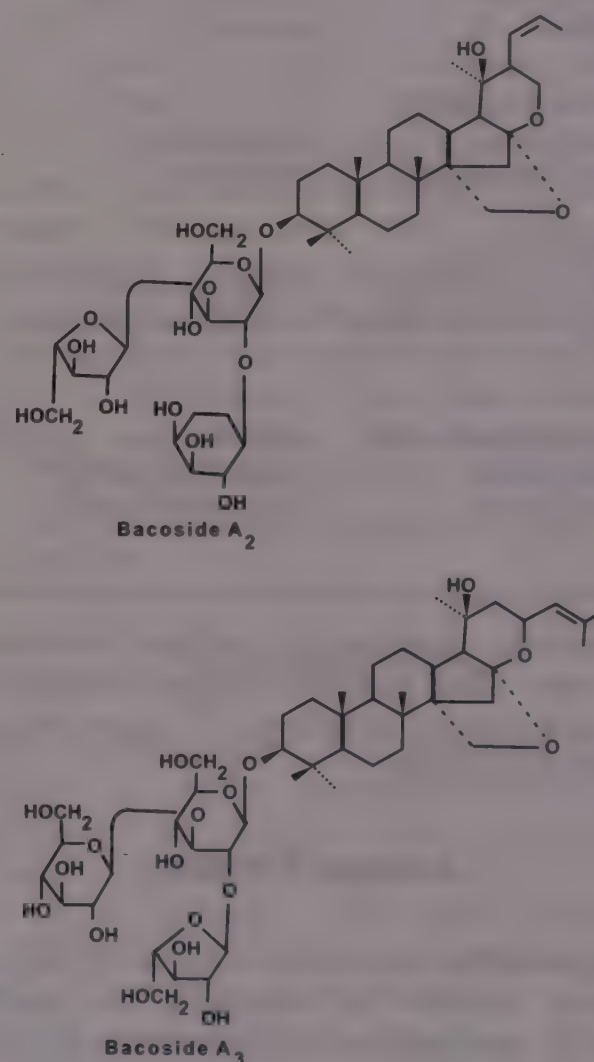


Figure 1. Chemical structure of the main active constituents of *Bacopa monniera*

### Clinical Studies

Several clinical studies have been done with drugs which are used to treat CNS disorders in Ayurvedic practice. The main advantage of such studies is that the patients can be diagnosed according to Ayurvedic criteria, the



drugs can be prepared according to Ayurvedic guidelines, and the effects can be evaluated. In the case of active Ayurvedic products, chemical and pharmacological studies can be initiated to isolate the effective compounds and determine their activity profile. The chemical constituents can then be used to standardize the Ayurvedic product or can be developed as new modern drugs.

The WHO guidelines for the assessment of herbal medicines now state that if a product has been used traditionally without demonstrated harm, then no specific restrictive actions should be taken.<sup>33</sup> Even though it appears to be a very rewarding approach, there are some limitations in the majority of published clinical studies. For example, clinical studies are generally open trials using a small sample size. Inadequate details of drug standardization are reported, and clinical effects are seldom assessed using Ayurvedic criteria. In spite of these limitations, a few leads have been obtained from the clinical studies and, in some cases, have been followed up by animal experiments. These trials are briefly summarized as follows.

*Mucuna pruriens*. -The seeds are used as a nerve tonic and some Ayurvedic physicians use it for the treatment of infertility.<sup>34</sup> A well planned clinical study by Vaidya Ashok and his colleagues showed that its activity in patients with Parkinson's Disease.<sup>35</sup> Vaidya Rama demonstrated the efficacy of the seed powder in antagonizing chlorpromazine-induced elevations in prolactin secretion, as is typically seen with L-dopa.<sup>36</sup> Earlier chemical studies had demonstrated that the seeds contain 5-6 percent L-dopa.<sup>37</sup>

Subsequent pharmacological studies have indicated that the seed powder is totally devoid of any effects on the cholinergic system<sup>38</sup> (quoted from reference 40). It has been shown in animal studies that the antiparkinsonian activity of the seed powder is not entirely due to L-dopa, because the L-dopa-free fraction also has significant antiparkinsonian activity.<sup>39</sup> Recent animal studies indicate that the seed powder has a more rapid onset of action and is more active than L-dopa.<sup>40</sup> It is likely that certain as yet unidentified substances contribute to the improved antiparkinsonian activity and greater tolerability of the seed powder in

comparison to L-dopa. Pharmaceutical preparations of *Mucuna pruriens* seed powder are now marketed in India, and the suggested dose is 5-10 g three times daily.<sup>41</sup> *Mucuna pruriens* seed powder has also been used in combination with *Withania somnifera* to treat depression.<sup>42</sup>

*Centella asiatica*. -This is one of the plants reputed to improve memory and intelligence in India<sup>43</sup> and in certain other countries.<sup>44</sup> Clinical interest was aroused following reports of its sedative action and hypothermia in animal studies.<sup>45</sup> Rao et al.<sup>46</sup> reported significant improvement in behavior and intelligence of 30 mentally retarded children in a placebo-controlled double blind study.

Varying degrees of improvement have been reported in other studies.<sup>47-48</sup> In normal children, *Centella asiatica* had no effect in a placebo-controlled 1-year study.<sup>49</sup> It has also been reported to be useful in the treatment of anxiety neurosis. An anti-anxiety and an anticonvulsant action have been demonstrated in subsequent animal studies also.<sup>49-52</sup> Even though several compounds have been isolated and characterized their CNS effects have not been studied, and they merit attention.

*Convolvulus pleuricalis*. -This plant is extensively used as a brain tonic in Ayurvedic practice and is a constituent of many over-the-counter preparations. An open trial has been reported in 30 cases of anxiety, with significant symptomatic relief following a month's therapy. Mental functions also showed a significant improvement.<sup>53</sup> In experimental studies, an ethanol extract of *Convolvulus pleuricalis* exhibited CNS depressant and hypotensive activities.<sup>54-56</sup> A more detailed clinical and experimental evaluation of the plant is needed. Even chemical studies appear to be limited.

*Celastrus paniculatus*. - The seeds and oil are used in Ayurveda to stimulate intellect and promote memory.<sup>57</sup> The clinical reports are conflicting, however, partly due to the use of different preparations. The oil has been reported to facilitate learning<sup>58</sup> and has also given promising results in psychiatric practice.<sup>57</sup> On the other hand, in a double blind study, Morris et al.<sup>59</sup> found the seeds to have no effect on learning in mentally deficient persons. In experimental studies,



the oil was found to have tranquilizing and anticonvulsant activity;<sup>60</sup> these activities were localized to a chromatographic fraction Mal-III.<sup>61</sup> Further fractionation did not improve the activity. Chemical characterization of the fraction has been done.

*Withania somnifera*.—The plant enjoys a reputation as a brain tonic. However, clinical trials with this plant have been limited. In an open trial of 30 cases of anxiety neurosis, a significant improvement was reported in anxiety level, mental work, and immediate memory span.<sup>62</sup> It has also been reported to reduce augmented urinary excretion of tribulin, considered to be a specific marker of stress.<sup>63</sup> It has also been used clinically in combination with *Mucuna pruriens* for the treatment of depression. An alcohol extract of the plant potentiated barbiturate hypnosis and reduced spontaneous motor activity in rats.<sup>64</sup> The results are in agreement with earlier studies using the total alkaloid fraction.<sup>65</sup> Chemical studies have revealed the existence of four distinct chemotypes mainly differing in the relative proportion of various withanolides.<sup>66</sup> This finding should be taken into account when conducting further experimental or clinical studies.

### Broad-Based Screening

The Central Drug Research Institute in Lucknow has been involved in broad-based screening of medicinal plants for over 25 years. The program includes a large number of tests for various types of CNS activities. The results of the screening efforts have been reviewed in the proceedings<sup>12</sup> of an earlier Indo-US Workshop held in Bangalore in 1993. The plants included a large number used in Ayurveda and other traditional Indian systems of medicine for CNS and peripheral diseases. A midterm analysis found that the percentage of active plants did not differ between a random sample of 1,200 plants with no prior biological or clinical data and a sample of 750 plants used in traditional systems.<sup>67</sup> This type of screening does not appear to be as rewarding as the use of more specific tests with plants whose clinical use for treatment of CNS disorders is well documented in Ayurvedic texts. Such plants

naturally deserve much greater attention.

### Concluding Remarks

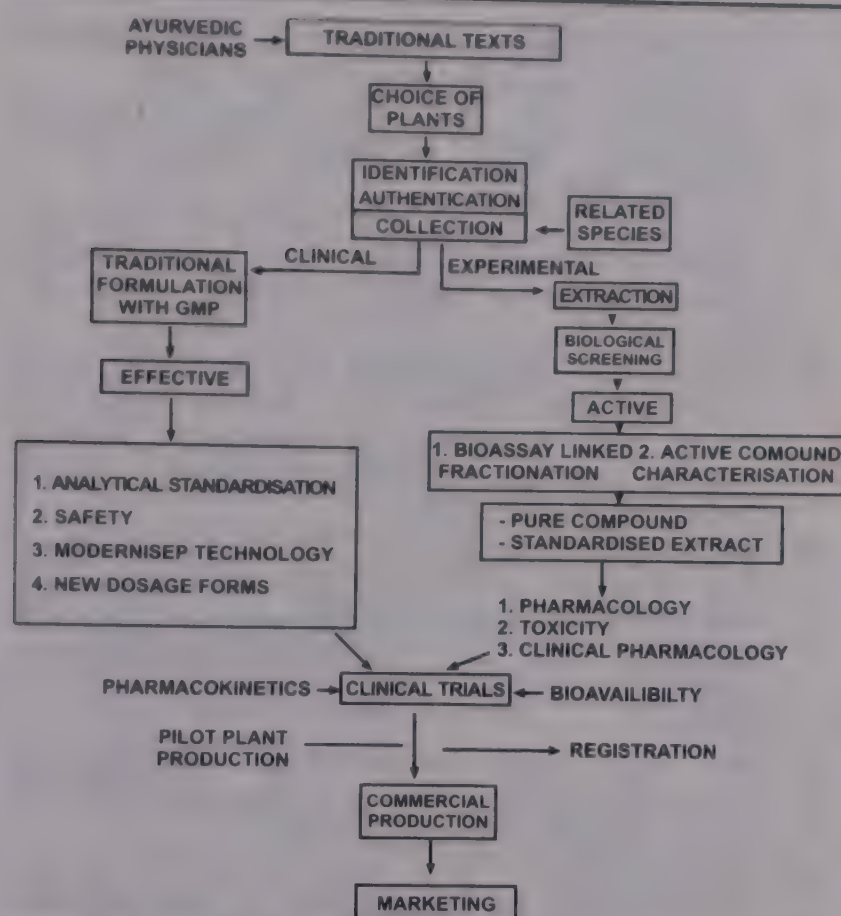
This review clearly indicates that the Ayurvedic Pharmacopoeia is a valuable resource in the treatment of CNS disorders. It is likely that initial clinical studies may be undertaken more expeditiously and that detailed chemical and biological studies can be done on selected plants.

It is remarkable that Colonel Sir R. N. Chopra had suggested this strategy in his classical treatise in 1933.<sup>68</sup> The test systems may have been refined since then, but the strategies have not changed. In my view, the objectives of research on Ayurvedic drugs should be threefold. Suitable Ayurvedic drugs should be standardized and manufactured using GMP (good manufacturing procedures) norms and used as such in the modern system of medicine. Second, in the case of plants where active compounds have not been yet isolated, a suitable natural constituent may be used as a characterizing compound. This has also been recently recommended by the WHO.<sup>69</sup> The third objective should be to develop active constituents as new drugs or to use them as leads for new semisynthetic or synthetic derivatives. These approaches have been summarized as a flow chart in figure 2.

Several problems which are encountered in testing Ayurvedic drugs and various fractions from active plants in animal systems are unavailability of adequate quantities initially and the large number of chromatographic (or other) fractions to be tested. Mechanism based screens<sup>70</sup> using *in vitro* enzyme or receptor assays may prove very useful for this purpose. There has been little effort to harness them.

Finally, I would like to make a plea for the use of standardized extracts rather than single pure compounds from active plants. Plants usually produce a family of closely related compounds whose activities differ only quantitatively; these compounds exert a synergistic effect. Extracts can be standardized on the basis of the major active constituents. Mention has been made in an earlier section about the greater activity of *Mucuna pruriens* extract in comparison to





**Figure 2. Flow sheet of two viable approaches for the development of Ayurvedic remedies.**

L-DOPA. Similarly, with *Bacopa monniera*, the total bacosides are as active as a single compound, the extraction procedure is simple and economical, and the yield is high. In many cases, extracts are better tolerated than single compounds. Thus, extracts of *Rauwolfia* are still used therapeutically and perform better than the single alkaloid, reserpine. This is true not only for CNS plants but for other classes of plant-based drugs as well. We have published our studies with several plants, including the hypotensive *Coleus forskohlii*,<sup>4</sup> the hypolipidemic *Commiphora wightii*,<sup>71</sup> the hepatoprotective *Picrorhiza kurroa*,<sup>72</sup> and the macrofilaricidal *Streblus asper*.<sup>73</sup> According to the data from the pharmaceutical industry, the generation of new lead compounds accounts for about 30 percent of the total cost of new drug development.<sup>74</sup> It has been aptly said about drug research, "Travellers, there are no paths, paths are made by walking." In the case of Ayurvedic drugs, the paths have already been made.

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### **Ayurvedic Classification of CNS-activity**

Vedanasthapana-Analgesics	Swapnajanana - Sedatives
Mastiskavasadana - Depressants	Smritihara - Amnesics
Sangnahara - Anaesthetics	Saumanasyajanana - Mood elevators
Medhya - Intelligence enhancers	Mastiskaprasadana - Stimulants
Rasayana - Rejuvenators	Vata - Sanasamana - Neurobalancers
Mohajanana - Confusants	Nidrashaman - Antisleep
Shokahara - Antidepressants	Smritikara - Memory enhancers
Sangnasambodhana - Consciousness - restoring	Unmadahara - Antipsychotics
Apasmaranuta - Antiepileptics	Madak - Intoxicants
Vayasthapana - Antiaging	Vata - prakopana - Neurodisruptive

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### **Ayurvedic CNS - active formulations :**

- |                              |                        |
|------------------------------|------------------------|
| 1. Khanda Kushmandavaleha    | 10. Brahmvati          |
| 2. Brihat Vatachintamanirasa | 11. Smriti Sagar Rasa  |
| 3. Mahayograj Guggulu        | 12. Saraswatarishta    |
| 4. Mahanarayana Taila        | 13. Praval Panchamrita |
| 5. Lakshminarayana Rasa      | 14. Swarn Bhasma       |
| 6. Vatagajendrarasa          | 15. Balarishta         |
| 7. Brihat Kasturi Bhairava   | 16. Ashokarishta       |
| 8. Krishna Chaturmukha       | 17. Chyavanprasha      |
| 9. Makardhwaja Rasa          | 18. Vatarirasa         |

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# Psychiatric Problems in Purview of Ayurveda and Their Treatment

V. N. Pandey

The industrial and technological revolutions have brought about an admixture of virtues and vices. Vices such as unfair competition, survival of the fittest, and killer instincts, have resulted in mental stress, strain, anxieties, aberrations, and physical and mental disorders. Ayurveda is an ancient system of Oriental medicine with rich philosophical undertones. It copiously draws ideas from Vedas and Darsanas such as Vaiseshika, Sankya, and Yogapathanjala and tries to restore man to an eternal, blissful state.

## Manovikaras in Ayurveda

The living person is a combination of Sarira (body), Indriya (senses), Satva or Manas (mind), and Atma (soul). Of these, Sarira (body) and Manas (mind) are affected by the Tridoshas (the elements, Vata, Pitta, and Kapha) and the Dwidoshas (the elements Rajas (passion) and Tamas (inertia)). Vata-Pitta-Kapha are referred to as Saririka Doshas (physical elements), and Rajas-Tamas are referred to as Manasika Doshas (mental elements).

Even though mental diseases such as Unmada (psychosis) and Apasmara (epilepsy) also affect the body, they are classified as Manovikaras (mental illnesses) because of the involvement of Rajas and Tamas as causative factors. Generally, mental disorders consist of the following four types:

- *Kevala (Manoadhishthita) Manovikaras-emotional/neurotic disorders*

The mental disorders such as Kama (passion) and Krodha (anger) are examples of this type. The Kevala Manovikaras are caused by Rajas-Tamas (the mental elements, passion-inertia).

- *Nanatmaja Manovikara-somatized conditions*

These mental disorders are caused exclusively by the involvement of one of the Saririka Doshas (physical elements), namely Vata-Pitta-Kapha. Aswapna (insomnia) and Anavasthita Chittatva (fickle mindedness) are examples of this type.

- *Sariramanoadhishthita Manovikara-somato-psychic conditions*

These types of disorders are characterized by an initial affliction of the body followed by a secondary affliction of the mind. Unmada (psychosis) and Apasmara (epilepsy) are examples of this type.

- *Manosariradhishthita Manovikara-psycho-somatic/somaticized neurotic states*

In this type, both the mind and body are afflicted concomitantly. For example, different kinds of Jwara (fever) and Atisaras (diarrhea) caused by Shoka (sorrow/ grief, Bhaya (fear), and so forth affect both the mind and the body. In this type, the mind is initially affected and then the body.

Sariramanoadhishthita and Manosariradhishthita are referred to together as Ubhayatmaka (dual type mind/body conditions). Some of the Nanatmaja manovikara can be included in the Sariramanoadhishthita manovikara because the causation and treatment of these conditions are similar.

## Nidana (Etiology or Causative Factors)

- Aharajanya (caused by food)
  - Visamahara (irregular food habit)
  - Viruddhahara (incompatible food)
  - Paryushitahara (stale food)
  - Malinahara (dirty food)
  - Asatmyahara (unwholesome food)
- Viharajanya (caused by habits)
  - Atijagarana (excessive wakefulness)
  - Atimaithuna (excessive sexual indulgence)



- - Deva-Guru-Dwija Apamana (disobedience/disrespect to God/teacher/ learned scholars)
- Manobhigata (emotional disturbances) such as Kama (desire/lust), Krodha (anger), Lobha (greed), Moha (delusion), Raga (infatuation), Dwesa (hatred), Irshya (envy), Abhimana (ego)

### Samprapti (Pathogenesis)

- Dusta Ahara-Vihara (Nidana Sevana)
  - Asatmyahara (unwholesome food)
  - Manobhigata (emotional disturbances)
  - Pragnaparadha (volitional transgression)
- Sarira (Vata-Pitta-Kapha)
  - Dosha Dusti (state of vitiation of the Doshas)
  - Manasa (Rajasa-Tamasa) (mental elements, passion-inertia)
  - Manovahasrota Dusti (vitiation of the sense of touch)
  - Manovikara (mental illness)

### Cikitsa Sutra (Treatment Principles)

- Virecana (purgation)
- Basti (enema)
- Nasaya (nasal instillation)
- Abhyanga (anointing)
- Takradhara (streaming of medication)
- Ksiradhara (buttermilk/milk/oil)
- Tailadhara (decoctions of herbals)
- Kashayadhara (medicines on the forehead)
- Mastiska Lepa (application of medications)
- Siro Lepa (application of wet cakes on the head and vertex)

### Cikitsa (Treatment)

- Daivavyapashraya Cikitsa (spiritual or divine therapy)
  - Mantra (incantation)
  - Ausadhi Dharana (application of medicines)
  - Mani Dharana (wearing herbs, sacred gems, etc.)
  - Mangala (propitiation)
  - Bali, Upakara (ablutions or offerings)
  - Homa, Niyama (sacrifice, vows)

- - Prayascita, Pranipata (penitence and prostrations)
- Yuktivyapashraya Cikitsa (biological or diet-drug therapy)
  - Ahara (diet)
  - Ksira (milk)
  - Ghrita (ghee)
  - Draksa (grapes)
  - Panasa (jackfruit)
  - Brahmi (*Centella asiatica*)
  - Mahisa Mamsa (buffalo meat)
  - Sarpa Mamsa (snake meat)
  - Barhi Mamsa (cuckoo meat)
  - Kurma Mamsa (tortoise meat)
  - Kakamaci (*Solanum nigrum*)
  - Vastuka (*Chenupodium album*)
  - Mahakusmanda (ash gourd)
  - Kapittha (wood apple)
  - Matulunga (*Citrus medica*)

### Ausadha (Medicines)

- Single Drugs
  - Brahmi
  - Vaca
  - Sarpagandha
  - Jatamansi
  - Tagara
  - Bala
  - Asvagandha
  - Satavari
  - Kusmanda
- Compound Drugs
  - Brahmi Ghrita
  - Kalyanaka Ghrita
  - Panchagavya Ghrita
  - Saraswatarista
  - Asvagandharista
  - Saraswata Curna
  - Smrtisagar Rasa
  - Caturmukha Rasa
  - Brahmyadiyoga
  - Ksirabala Taila
  - Dhanwantra Taila
  - Asanabilvadi Taila
- Rasayanas (tonics)
  - Aswangandha Curna
  - Kusmanda Rasayana
  - Cyavanaprasa
  - Brahmi Rasayana
  - Aswagandhavaleha
  - Satavari Leha



### **Satvavajaya Cikitsa (Psychotherapy)**

To restrain the mind from unwholesome objects by measures of :

- Yoga practices
- Dhyana (meditation)
- Japa (chanting sacred incantations, etc.)

### **Clinical Trials of the Council**

Three important clinical trials conducted by the Central Council for Research in Ayurveda and Siddha related to mental and neurological disorders are described below.

#### **Manas Mandata (Mental Retardation)**

Mandukaparni (*Centella asiatica* Linn.) leaf powder was administered at a dose of 6 g/day for 90 days to 30 mentally retarded children in the age group 3 to 15 years. The improvement in IQ value using the Binet-Kamat test battery showed a statistically significant improvement in the IQ and in General Mental Ability.

### **Chronic Unmada (Schizophrenia)**

Brahmyadiyoga, a compound drug, was used in 14 chronic Unmada patients of either sex, in the age group of 18 to 40 years, who had been suffering from chronic Unmada for 2 to 8 years. The dose of the drug was 8-16 g/day for 3 months. Assessments were done independently by an Ayurvedic physician, psychiatrist, and clinical psychologist. Seven of the ten patients who underwent treatment for 3 months improved. Four patients who took the drug for 2 months also improved.

### **Apasmara (Epilepsy)**

A compound drug (code name, Ayush-56) combining the extracts of Jatamansi (*Nardostachys jatamansi*) and Sunisannaka (*Marselia minuta*) was administered to patients suffering from Apasmara. The dosage given was two 500-mg tablets TID for a period of 3 years in 273 cases of Apasmara. The drug was shown to be an antiepileptic and a sleep inducer with no side effects.

"Changes in the system and in society will not change us people very much. I am the problem, and when I take responsibility for my own problems, even if they are determined by the environment - when I solve them and in this way transform society from inside out - I will be somebody else."

"In psychiatry too, the far-reaching reforms that have taken place in the last decades have remained on the surface. This is revealed in the fact that there are still massive taboos against true psychotherapy, that psycholytic therapy is still forbidden, that body work is still laughed at and that traditional adaptive psychiatry, which holds up the system still takes up most of the space".

- Samuel Widmer



# Ayurveda and Cultural Concepts of Mental Illness

M. Weiss

Ayurveda, the Hindu system of medicine, developed in the Indian subcontinent and remains widely practiced in India and Sri Lanka. It has also been practiced in Southeast Asia and more recently has been introduced in Western countries as a combined result of the South Asian diaspora, persisting questions about effective alternatives to mainstream allopathic medicine, integration with new-age health services, and aggressive marketing. Deeply embedded in the Hindu culture of its origins, Ayurveda is both a reflection of that culture in areas of health and medicine and a determinant of beliefs and practices affecting many other facets of life, especially diet, hygiene, and lifestyle.

The medical tradition is notable for a systematic account of diseases, including mental illnesses, based on a coherent medical theory. Comparative and historical study of the relationship between mental disorder in Ayurveda and ideas about insanity in other Hindu cultural traditions -such as religion, philosophy, law, politics, and literature-shows how culture, medicine, and psychiatry interact. Study of Unmada, the preeminent category of severe mental disorder in Ayurveda, and related concepts in the other Hindu cultural traditions shows how the system evaluated and treated these patients and clarifies cultural meanings of mental disorder and insanity.

Ideas about psychiatric nosology within allopathic psychiatry have changed dramatically in recent decades. At the same time, confrontation with the complexity of efforts to develop an international psychiatry have enhanced respect for the significance of cultural variation and the influence of cultural context on both psychopathology and the configuration of particular disorders, highlighting the importance of cross-cultural research. Without an adequate appreciation of the embeddedness of medical and psychiatric concepts in the cultures and

historical periods that produced them, comparative analysis of ethnomedical concepts, especially studies of Ayurveda, are likely to be simplistic. Even though considerable effort has been expended so that Western concepts embodied in the American Psychiatric Association's Diagnostic and Statistical Manual (DSM) and the International Classification of Diseases (ICD) may serve as international standards, these nosologies should be recognized as ethnomedical as well.

Ayurveda is not just a matter of historical interest; It remains influential as a system of medical practice, as a commercial pharmaceutical industry producing curative medicines and products for health maintenance, and as a cultural system that influences the way people think and behave. Because mental health professionals need to understand their patients' ideas about and experience of illness, and because clinicians also need to make themselves understandable, appreciation of the principles of Ayurveda confers practical benefits for practitioners of allopathy in India; it also offers valuable insights for mental health professionals and social scientists elsewhere.

## Ayurveda in the Classical Tradition

The primary sources of information about Ayurveda are a series of authoritative texts written in Sanskrit. Anthropological study identifies beliefs and practices associated with health and illness that may be consistent with the texts or diverge, clarifying patterns of continuity and change within the tradition. Research on Ayurveda has been undertaken by scholars and scientists working within and outside the system from various disciplinary vantage points. Philologists, clinicians, health scientists, anthropologists, historians, political scientists, and others have contributed to our understanding of Ayurveda as a

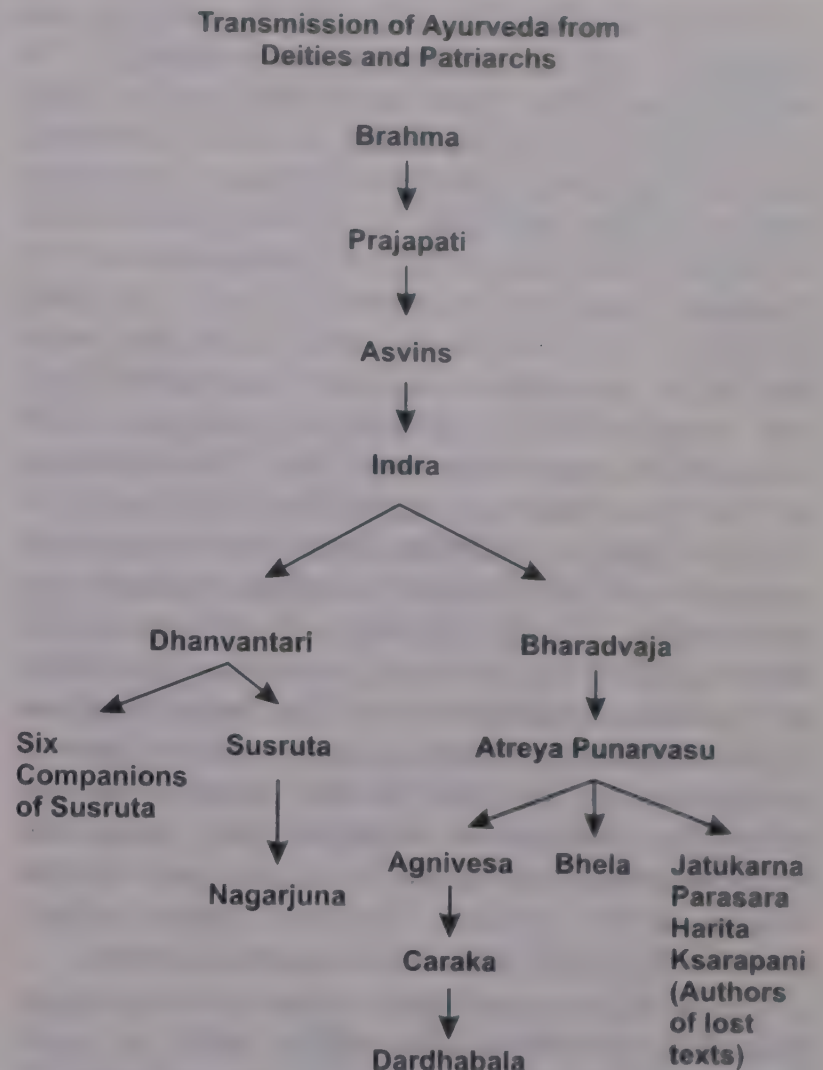


medical system, social institution, and cultural institution.

The Sanskrit texts are difficult to date, in part because the present editions include piecemeal contributions over an extended period, indicating a process of transformation. Scholars currently estimate the earliest of these texts were written between 200 B.C.E and 400 C.E., codifying a medical tradition that had been evolving orally several centuries previously. Vital links have been lacking to explain the gap in the style and premises of medical writing in the Veda and the professional systematized accounts of the Ayurveda. Recent scholarship suggests an explanation for this transition-which appears to fulfill criteria for what science historian Kuhn has termed a paradigm shift -may be found in the narratives and records of Buddhist mendicants in the Buddhist tradition. From historical research of Zysk, these accounts from the first 9 centuries B.C.E., written in Pali, may yet clarify the otherwise obscure transition from Veda to Ayurveda.<sup>1</sup>

The treatises of Ayurveda themselves trace their origins to divine sources, recounting a passage from Brahma to other deities and then either through Dhanvantari (lord of medicine in Sushruta or Bharadvaja in Charaka and Bhela) to the patriarchs of Ayurveda who produced each of the major texts (figure 1). Each of these texts-which include *Charaka Samhita*,<sup>2</sup> *Sushruta Samhita*,<sup>3</sup> *Astangahrdaya Samhita*,<sup>4</sup> and *Bhela Samhita*<sup>5</sup> - provide slightly divergent accounts of this transmission, and they each emphasize slightly different aspects of the medical tradition. The treatise of Sushruta, for example, gives weight to surgery, which is for the most part ignored by the others. As with other Sanskrit traditions, the work of commentators became associated with the original works, providing some indication of how the understanding of medical concepts changed over time.

The Vedic *Samhitas* are the earliest of the sacred books of Hinduism, written in Vedic, a more highly inflected and more complex language that preceded the classical Sanskrit of the Ayurvedic treatises. They and other literature associated with each of the four *Samhitas* (*Rig Veda*, *Yajur Veda*, *Sama Veda*, and *Atharva Veda*<sup>6</sup>) also deal with medical



**Figure 1. Transmission of Ayurveda from Deities and Patriarchs**

problems. Their approach, however, is less from a medical perspective grounded in medical theory, like Ayurveda, than a collection of magicoreligious hymns suggesting rituals, presented *ad hoc*, which produced their desired effects through supernatural means.<sup>7 8</sup>

Ayurveda is linked to classical systems of Hindu philosophy in much the same way that Western medicine (allopathy) is linked to philosophy, ethics, and basic life sciences such as biochemistry, biology, anatomy, and physiology. The six systems of classical Hindu philosophy are also regarded as liberation doctrines. Among them, Yoga is most closely associated with medicine. Despite considerable differences in their detail and application, it is primarily the six systems of formal Hindu philosophy, of which Yoga is one, that provided a vocabulary and conceptual frameworks that served as starting points for elaboration of the humoral theory of Ayurveda.



The three Doshas, which constitute the elements of a humoral physiology, or pathophysiology when the balance gives way to imbalance, are identified with wind (Vata), bile (Pitta), and phlegm (Kapha). Medical problems are typically characterized by the nature of this humoral imbalance, its location, and a specific disease process (Vyadhi). Although references to the term Dosha, if the terms are even mentioned, are not used with the technical meaning they have in the Ayurvedic tradition, the influence of conceptualizations of the three Gunas from the Samkhya tradition and the elaborate categories of the Nyaya-Vaisesika systems are discernible in the theory of Ayurveda.<sup>2 9</sup> References to the Gunas persist in Ayurveda as elemental substances of the mind-passion (Rajas), lethargy (Tamas), and clarity (Satva), analogous to the role of the Doshas in the body. The discussion of personality formation in Ayurveda, contained in a section of the major texts called Sarirasthana, refers extensively to the properties of the Gunas.

Each of the Ayurvedic texts refers to eight branches of medical knowledge, with no more than slight variation among them (table 1). This account is so clearly identified with Ayurveda that a reference to the eight branches, Astanga, is synonymous. Although each of the texts refer to the same eight categories, they tend to specialize in one or two. There are references to other texts devoted exclusively to topics among the eight categories, but none for Bhuta Vidya, under which mental disorders are typically included. Historian Majumdar<sup>10</sup> points out that no special treatise on this topic, unlike others of the eight branches, has been quoted or even named in the surviving works.

Notable among the sources for study of Ayurveda is Sharma's comprehensive study of the history of medicine in India.<sup>11</sup> Sharma completed this work after retiring as the Director of the Postgraduate Institute of Medical Research at Banaras Hindu University. It is an edited volume with contributions from leading scholars, whose approaches to Ayurveda are in some cases quite different. The book covers the pre-Vedic, Vedic, and post-Vedic periods, giving most attention to the last. Majumdar's work,<sup>10</sup> clearly written and well researched,

**TABLE 1.** -Eight branches of Ayurveda  
Astanga

<i>Kayacikitsa</i>	General medicine: Causes, diagnosis, and treatment of general medical disorders.
<i>Salyatantra</i>	Surgery: Recognition of disorders requiring surgical treatment and the use of surgical instruments to treat them.
<i>Salakyatantra</i>	Ophthalmological and related conditions: Treatment of diseases of the eyes, ears, nose and throat, originally a specialty branch of ophthalmological surgery.
<i>Bhutavidya</i>	Possession or possession-like states: Disorders associated with supernatural origin, but also including mental illness and epilepsy.
<i>Kaumarabhrtya</i>	Pediatrics: Diagnosis and treatment of childhood disorders.
<i>Agadatantra</i>	Toxicology: Treatment of poisoning of all kinds, including mineral, vegetal, and animal poisons; snakebites and other venoms.
<i>Rasayana</i>	Health maintenance and enhancement: Tonics for promoting long life, good health, strength, and well-being.
<i>Vajikaranatantra</i>	Sexual functioning: Treatment or enhancement of virility and sexual potency.

provides an account of Ayurveda in a volume that places it in the context of other Indian scientific traditions (see also reference 12). Also based on the Ayurvedic treatises, a chapter by Basham studies the social history of the physician (Vaidya) in Ayurveda, with accounts of training, medical practice, ethics, the role of hospitals, and patronage by the king.<sup>13</sup> The first volume of Mehta's five-volume translation of the *Charaka Samhita* also provides a detailed account of the social history of medicine, gleaned from passages in Charaka and the other treatises.<sup>2</sup>

Jolly's monograph on Ayurveda, published at the beginning of the present century, written in German and translated into English by



Kashikar, continues to serve as an excellent source book for studying textual accounts of various diseases according to Ayurveda, notable because it draws so carefully on texts that are still untranslated into Western languages, such as *Astanga Samgraha*.<sup>14</sup> Textbooks for teaching the practice of Ayurveda written by medical scientists and teachers at Ayurvedic medical colleges, such as Dwarkanath, indicate how Ayurveda is presently taught and in some instances how allopathic concepts are presently integrated into current practice.<sup>15</sup>

### **Ayurveda, Science, and Practice**

A number of anthropological studies of Ayurvedic practice, based on fieldwork in communities, clinics, and with practitioners, help to clarify the relationship between theory and practice; they also indicate how Ayurvedic concepts are translated into practice by practitioners and how they are understood by laypersons in the community. Zimmermann's study from ethnographic field experience with an Ayurvedic practitioner and scholar, Vayaskara Mooss, in Kerala demonstrates the value of considering both textual and ethnographic perspectives.<sup>16</sup>

Trawick's ethnography of a healer in Tamil Nadu clarifies fundamental differences in the ways by which knowledge is acquired in Ayurveda and allopathy with reference to the meaning of science in Ayurveda.<sup>17</sup> Her analysis considers the implications of relying on the past orientation of revealed texts or the future orientation of research findings in allopathy as the source of knowledge within the system. She argues that the textual basis of knowledge is consistent with the role of the Ayurvedic physician as scientist and consistent with intellectual struggle and open competition among rival theories, as well as open to challenges from nature.

Obeyesekere also tackles these questions about empiricism, science, and what constitutes a scientist with reference to Ayurveda, illustrating his argument with case studies from fieldwork in the practice of an Ayurvedic practitioner in Sri Lanka.<sup>18</sup> His work shows how clinical practice involves a kind of clinical experimentation. Although Ayurveda

is "grounded in well-recognized procedures of validation and experimentation," he argues that "there are no professional scientists of Ayurveda, that is, those whose main role is the generation of scientific knowledge through research" (p. 162). While these arguments are framed mainly with respect to the philosophy of science and medicine, they have practical implications that affect the institutional structures and the values that are reflected in teaching and practice and affect the maintenance of the tradition. Political overtones of persisting questions about the appropriate acquisition of knowledge, that is, the epistemology of Ayurveda, have fueled a vigorous debate within the tradition in India. Are revealed texts or research findings more authoritative? Such questions are also at the center of controversy about whether the field should remain "pure" (Suddha) with respect to the texts, or whether it should encourage integration of allopathic and Ayurvedic ideas and practice.

For many years, the Government of India through various agencies, including the Central Council for Research in Ayurveda, Unani, and Siddha, the three recognized indigenous systems of medicine, has supported research on pharmacognosy, with extensive pharmacological analysis of herbal substances used in Ayurveda. The present Director-General of the Indian Council of Medical Research (ICMR), G. V. Satyavati, was trained in Ayurveda. In a previous capacity as editor of the ICMR Journal, she prepared a volume that reviewed various activities in the field of Ayurvedic research.<sup>19</sup> These institutionally supported, knowledge-generating activities, quite distinct from the clinical empiricism of the individual practitioner, are well represented in academic medical centers, like Banaras Hindu University, and published in journals that report findings from research on Ayurveda. The literature on Ayurvedic clinical research studies is enormous. Whether or not one may wish to criticize or acclaim the quality of this research, the magnitude of these activities suggests that from his study of a clinical practitioner, Obeyesekere may have generalized inappropriately by concluding that professional scientists of Ayurveda do not exist.

Other writing about Ayurveda includes the immense body of literature for lay audiences,



providing advice for improving health and curing ailments that can be treated without medical consultation. Publications from Ayurvedic clinical research studies, health educational literature appealing to a popular audience,<sup>20</sup> and a mass of advertising and marketing literature, constitute important sources of information, not just for people who want to know how to make use of Ayurvedic advice and products, but also for social scientists; this literature shows how Ayurveda has adapted to conditions in the present day, both in its culture of origin and in Western cultures engaged in the process of incorporating it. A large body of information about Ayurveda is available on World Wide Web pages through the Internet, including literature about Ayurveda, views of various health problems, information about courses, and products that may be purchased over the Internet.

### **Role of Mental Health in Ayurveda**

Ayurveda acknowledges the importance of both mental and physical aspects of health, and the role of both mind and body are recognized as determinants of diseases. Health maintenance and disease prevention, however, focus more on physical rather than mental health.<sup>21</sup> Passages speaking to mental health and well-being advise that peace of mind follows as a benefit of lifestyle. Despite the holistic character, which modern interpreters of the tradition emphasize, it is notable that the distinction between *Mansik* (mental) and *Saririk* (bodily) is well understood, more similar in that regard to Western than Chinese formulations of mind and body, which are difficult even to specify in Chinese languages. But in their relationship with respect to the specifics of health and disease in Ayurveda, the emphasis on *Mansik* is clearly less.

Passages dealing with values of mental wellbeing are scattered throughout Ayurvedic texts, mainly in the sections on theory and practice that refer to the general principles derived from aspects of other Hindu cultural traditions. These discussions acknowledging the bodily and mental determinants of disease are found mainly in the first sections of the treatises, *Sutrasthana*: "The body and that which is understood as the mind are both the

mainstay of disease as well as the well being" (1.1.55). Passages such as these are typically cited as the basis for an emphasis on a holistic perspective in Ayurveda.

Considered in the context of the discussion on *Unmada*, mental well-being focuses on the benefits of appropriate diet and lifestyle. The section on the therapeutics of *Unmada* in the *Charaka Samhita* concludes with the following passage:<sup>2</sup>

One who avoids meat and intoxicating  
beverage,  
who desires what is wholesome and is  
pious and pure,  
This clear-headed one contracts neither  
endogenous (*Nija*) nor exogenous  
(*Agantu*) *Unmada*.

(6.9.96)

### **Cultural Concepts of Mental Health**

Other Hindu traditions, especially Yoga, are more explicit in their attention to the goals of achieving freedom from the conflicts and burdensome thoughts that may be associated with the stream of mental activity (*Citta Vritti* in the *Yoga Sutra*<sup>22</sup>) and the attainment of peace of mind. The lack of stigmatized associations with mental illness and resonance with the values of widely accepted spiritual ideals help to explain the attractiveness of these preferred alternatives to Ayurveda for enhancing mental well-being.

Questions about mental health, defined mainly with reference to striving for peace, equanimity, and release from the tensions of everyday life (characterized by the cycle of rebirth [*Samsara*]) are prominent values motivating a strong link between philosophy and liberation. The *Yoga Sutra*, the earliest and principal text of the Yoga system of philosophy, elaborates psychological concepts derived from the philosophical system known as *Samkhya*, which is associated with Yoga. A well-known passage of the *Yoga Sutra* explains at the outset that "yoga is the control of the flow of mental activity" (*yogascittavrtti nirodhah* [YS 1.21]).

This account is presented in the context of a prescription for a spiritual attainment, which in the Yoga tradition is known as *Samadhi*: it is a positive attainment, rather than a means of overcoming psychological distress or a mental



disorder. In its extreme form, this attainment is associated with supernatural powers (Siddhi), but its broad appeal is related much more to practical benefits of enhanced wellbeing and better health in everyday life. This emphasis on health is especially prominent in the later tradition, the Hatha Yoga, which elaborates a repertoire of yogic postures as the means for maintaining health and well-being. The later tradition and present-day applications of Yoga also advocate specific yogic practices as part of the treatment for certain diseases.<sup>23 24</sup> Even some allopathic hospitals in India have a Yoga department, which prescribes adjunctive Yoga therapy.

Writing about Yoga and medicine, Majumdar concludes:<sup>10</sup> "This integrated system of mental concentration, breath-control, sense-control and physical culture can also be called a medical system" (p. 235). Zysk, a Western historian specializing in the Vedic and Ayurvedic medical traditions, supports this view. He traces the development of offshoots of the doctrine of the bodily winds from Vedic sources into two distinct streams, one formulated as the concept of Vata in Ayurveda and the other leading to the emphasis on respiration among the techniques emphasized in the practice of Yoga.<sup>25\*</sup>

Today one finds that Yoga routinely employs the teachings and methods of Ayurveda in its spiritual exercises, while Ayurveda remains relatively free of Yogic doctrines, principles, and techniques. (p. 213).

Like Yoga, texts of the other Hindu systems of philosophy do not concern themselves with mental disorder and make at most a circuitous reference to Unmada or similar terms. They are deeply concerned, however, with suffering (Duhkha) as an existential problem, and they recognize the need for a sharp intellect capable of grasping the necessary insights to overcome

this suffering. Like others, Obeyesekere's study of psychological medicine in the Ayurvedic tradition emphasized the influence of concepts from the Samkhya system of philosophy.<sup>27</sup> A passage in the principle text of this tradition, the *Samkhyaa Karika* (49), identifies 17 varieties of injury to the intellect.<sup>28</sup> A later commentator, Gaudapada, includes Unmada among them, but without any further elaboration.

Another commentator, Veda Vyasa, on the *Yoga Sutra* (1.30) refers to a related but less severe condition, Pramada, which is often translated as infatuation or delusion-more in the sense of immaturity or weak character than a psychotic fixed false belief. Like other forms of disturbed thinking (Cittaviksepa), Pramada interferes with the aim of Yogic meditation, that is, attainment of Samadhi. This understanding of Pramada as an impediment to liberation resonates with ideas traceable to the speculative literature of the earlier Vedic tradition. In the *Katha Upanisad*, Yama, lord of the dead, warns:<sup>29</sup>

The passage at death to the other realm is not manifest to a child, to one who is deluded (Pramada) by infatuation with acquisitions, nor to a fool. (1.2.6)

The effort to relieve suffering by attaining liberation from the cycle of rebirths (Moksa) motivates these texts, giving them a practical aim to address the inherent suffering of the human condition, as it does even more clearly in the Jain and Buddhist traditions. References to the Buddha as the great healer (Mahavaidya) suggest a metaphorical equation of providing relief from suffering through liberation, termed Nirvana, and relief from disease through cure. Passages in the Pali Buddhist canon and postcanonical literature also refer explicitly to Unmada associated with arousal from a trance state and other contexts.<sup>30</sup>

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\* The medical status of Yoga is not just an academic point, since implications for governmental support if recognized as a medical system have long been recognized. In the preface to a report of a committee on evaluation of therapeutic claims of Yoga, the authors explain: "Proposals were received by the Government of India for financial assistance from nonofficial institutions to start hospitals and other centers where patients suffering from different diseases could be treated through 'Yogic Kriyas.' The Government thought it fit to have this aspect of Yoga examined scientifically and to work out financial assistance, if any, which should be provided for such institutions."<sup>26</sup>



From the Ayurvedic texts alone, because they lack case histories, it is difficult to appreciate the social meanings of mental illness. Like the medical texts of allopathy and clinical handbooks used by medical house officers, they focus more on the signs and symptoms that a clinician needs to know to make a diagnosis and guidelines for treatment. Clues about the social dimensions of mental illness, that is, Unmada and conditions specified by another term, Mada, which refers sometimes to a less severe disorder or to alcoholic intoxication, are found in other kinds of texts, such as the *Dharmasastra* and *Nitisastra*. These texts identify social circumstances in which persons affected with the condition are vulnerable and require protection.

For example, Narada Smṛti (17.17) advises that "taking [something] away from those who are sleeping, insane, or confused (Supta-Unmatta-Pramatta) through various ploys is theft."<sup>31</sup> Similarly, contracts made by them or gifts from insane persons are not considered valid. Another text advises that speaking falsely does not have the same consequences for the insane, intoxicated, aged, and other such persons (5.25).<sup>32</sup> As a practical matter, a text with advice on achieving success in worldly pursuits and statecraft, Kautilya's *Arthasastra* (4.4.1-5) advises that spies may be disguised as insane persons, among others.<sup>33</sup>

Many of the treatises of Hindu law and conduct group persons with Unmada with others who are similarly stigmatized by leprosy (Kustha) and epilepsy (Apsamara). For a highcaste Hindu, merely looking at such persons may be polluting. These conditions were sufficient to annul a marriage and disqualify affected persons from the rights of inheritance. Recognizing the serious social impact of these conditions, some of the texts specified that slandering someone by calling him insane was a punishable offense (3.18.1-6).<sup>33</sup>

Sanskrit literary traditions sometimes associate love and madness, especially the lover who is so anguished by the absence of the beloved as to become insane. The love story of Pururavas and Urvashi, a well-known and recurring theme in Sanskrit literature, is a good example. Pururavas was separated from his lover, Urvashi, by Indra, chief among the Vedic

gods. Pururavas then wandered about "like one insane" (Unmattavat) (7.150).<sup>34</sup> In another expression of this theme, one of the five arrows of Kama, the personification and god of love, is called Unmadana, because it is maddening. The Kathasaritsagara (15.65) includes the story of Unmadini, a young woman whose name referred to the fact that her beauty was so extreme that it drove any man who saw her to madness. When her father approached the king to offer her in marriage, explaining "I dare not give her away to anyone else, without informing your Majesty," the ministers became concerned about the welfare of the kingdom. "If the king gets hold of this maiden, the kingdom will be ruined, for his mind will be thrown off its balance by her, and he will not regard his kingdom; so we must not tell the king that she possesses auspicious marks."<sup>35</sup> In the most renowned of all Sanskrit dramas, *Sakuntala* is called Unmadayitr, the maddener, in Act 1, because King Dusyanta became crazed with love after seeing her.

The theme of a woman working her spell on a man by crazing him with love can be traced to the Veda in a hymn of the Atharva Veda (6.130). This love potion invokes the deities and natural forces to ensure that a man who has previously resisted will find the woman invoking the charm irresistible. It even goes a step further, releasing her from the attraction to him, so that she is unfettered as he is consumed by the passion of his attraction to her.<sup>6</sup>

This is the Apsarases'love-spell,  
the conquering resistless ones.  
Send the spell forth, ye Deides!  
Let him be consumed with love of me.  
I pray, may he remember me,  
think of me, loving and beloved.  
Send forth the spell, ye Deities!  
Let him be consumed with Love of me.  
That he may think of me,  
that I may never, never think of him.  
Send forth the spell, ye Detties!  
Let him be consumed with love of me.  
Madden him, Maruts, madden him.  
Madden him, madden him, O Air.  
Madden him, Agni, madden him.  
Let him be consumed with love of me.  
(6.130)



## Vedic Concept of Mental Disorder

The earliest discussion of an intervention for Unmada is found in the *Atharva Veda*. A single hymn in the treatise devoted to healing mental illness implores the god of fire, Agni, to free the affected person from madness. Gods and demons (Deva and Raksas) are regarded both as the cause of the disturbance and the source of healing.<sup>6</sup>

O Agni, release this man for me,  
he who bound and well secured chatters  
on and on,  
That he may thus attend to your sacrificial  
share  
when he shall become freed of madness.  
If your mind be crazed,  
let Agni calm it for you.  
Possessing the knowledge, I prepare a  
remedy  
so that you may be freed of madness.  
Maddened by the mischief of the gods,  
maddened by a demon.  
Possessing the knowledge, I prepare a  
remedy  
so that he may be freed of madness.  
May the Apsarases, Indra, and Bhaga  
return you,  
May all the gods return you  
so that you might be freed of madness.  
(6.111)

The hymn entreats the deity, promising that in return for cure, this person will be able once again to fulfill ritual obligations. The quasi-religious and quasi-medical overtones of this passage imply that the oblation and the medicinal preparation are complementary, indicating respect for the value of both. Although the emphasis shifts dramatically from the magico-religious in *Atharva Veda* to a professional medical framework in Ayurveda, this recognition of the value of each as complementary persists (see below).

Other Vedic passages refer to Unmada, but except for the *Taittiriya Samhita* (TM) (3.4.8.4), a text of the *Yajur Veda*, which recommends an offering of hot coals for an affected person, the others are not concerned with healing.<sup>36</sup> It associates insanity with

celestial musicians and their consorts (Gandharvas and Apsaras) and also with failure to properly perform the Vedic sacrifice (TS 5.5.1.2). The *Sama Veda* applies the term to a sacrificer who remains in the other world, suggesting a kind of trance state, rather than returning after the Vedic sacrifice. The *Rig Veda*, however, considers Unmada not so much as a disorder, but as the blissful state of euphoria that various deities, especially Indra, attain after ingesting soma, a psychotropic substance that figured prominently in the Vedic ritual.<sup>37</sup>

## Ayurvedic Concept of Mental Disorder

In the treatises of Ayurveda, much less space is devoted to mental, compared with physical, illness. Mada refers to intoxication or a preliminary phase of Unmada. Various other disorders have been identified by modern interpreters of the tradition, but they are not all found in all texts, and for many, other than Unmada, the passages that mention them are so brief and telescopic that they should more properly be taken as symptoms, rather than disorders. These include anger, greed, jealousy, and so forth.

All of the major texts regard Unmada, the term designating severe mental disorder, as a medical problem and discuss it in chapters on pathology (Nidana) and therapeutics (Cikitsa). They consider the general features, predisposing factors, and the nature of its psychological impact on perception (Indriya) and various formulations of the mind (Manas, Buddhi, and Hrdaya) (table 2). The elaboration of Unmada as a disease (Vyadhi) in the Ayurvedic texts indicates that it was clearly regarded as a medical problem, although the discussion of the exogenous type suggests that it is explained according to principles different from accounts of the endogenous type and most other diseases according Ayurveda.

The texts identify two broad categories of mental disorder: disorders associated with the imbalance of the three Doshas, which are termed endogenous (Nija), and those that are related to various classes of demons and deities, termed exogenous (Agantu) in Charaka and Bhela or demonic (Bhuta) in the others. Subtypes of the endogenous category relate



**TABLE 2.** -General features of severe mental disorder (*Unmada*) according to Atreya  
Punarvasu-Caraka Samhita (6.9.4-7)

Cause	Predisposing features	Mechanism	Symptoms
Prohibited, spoiled or unclean foods; Impact of gods, sages, and brahmans	Fear and terror in the stricken mind; Chaotic mental struggling; Lack of mental clarity	Pollution of the heart, where intellect (buddhi) resides, with toxic impurities (mala); Impurities flow to the mind and cause confusion	Disordered thinking; Loss of clarity; Confusion; Visual disturbances; Loss of confidence; Indiscriminate speech; Emptiness of the heart/mind (hrdaya); Bewilderment; Dispassionate, neither happy nor sad; Immoral behaviour; Wandering about with impaired memory, intellect, and awareness; Thoughts fly about

various somatic signs and symptoms and psychopathology with the disturbed balance of the Doshas, either singly or as a combination of all three (Sannipata), which has the most severe prognosis (table 3).

Accounts are for the most part similar in themajor texts, although Sushruta and Vagbhata's *Astangahrdaya Samhita* include two additional categories (namely, resulting from mental anguish from a stress, loss, or shock

[Sokaja] and poison [Visaja] that Charaka does not (Sushruta 6.62.4-5; Astangahrdaya 6.6.1,15-17). Bhela also acknowledges a type of Unmada caused by loss of wealth or bereavement (Bhela 2.7.g). Although Charaka does not identify Unmada due to stress, loss, or shock as a distinct type, the discussion of the exogenous type does refers to various periods of stress and vulnerability when an individual is most susceptible to the approach

**TABLE 3.** - Humoral Types of Severe Mental Disorder - Endogenous (*Nija*) *Unmada*  
Caraka Samhita 6.9.9-10, 25

Type	Cause or predisposition	Psychopathology	Somatic symptoms	Specific treatment
Wind type Vata	Dry, cold, or insufficient food; Purgation; Decay of body elements Fasting	Inappropriate laughing, smiling, dancing, etc; Emaciated and ragged;	Reddish complexion; Worse after eating	Unctuous beverage; Mild purgative if constipated
Bile Type Pitta	Foods that are indigestible, bitter, sour, or hot	Impatient, excited, threatening, agitated, angry; Nudity; Hallucinations	Yellow complexion; Feeling hot	Emetics, purgatives, oily massage, sudorifics; Enema, either unctuous or purging
Phlegm Type Kapha	Fullness in the stomach	Slowed speech and action; Excessive sleeping; Favors solitude, avoids wife	Loss of appetite; Nausea; White fingernails; Condition severe after eating	Emetics, purgatives, oily massage, sudorifics; Enema, either unctuous or purging



of various Bhutas.

Subtypes of the exogenous category relate psychopathological symptoms and behavior to the character of well-known classes of demons and deities (table 4). Etiology, discernible from evaluation of signs and symptoms, is the basis of classification for the endogenous (Nija) disorders. The account of perceived causes of the exogenous (Agantu) disorders, however, is

inconsistent and ambiguous, and there appear to be variations in the explanation not just from the earlier to the later texts, but also within some texts.<sup>38</sup> It is not clear whether these disorders actually specify possession states, as they clearly do in the Atharva Veda, or whether they refer to demons as a means of specifying particular forms of disturbed behaviors identified with personalities of demons and

**TABLE 4.** - Exogenous types (*agantu*) of severe mental disorder and associated spirits (*bhuta*)

Type	Cultural meaning	Premorbid features	Symptoms	Onset
Deva	Gods - divine and authoritative	Pure, experienced in austerities, and studious; Moral; Dressed in white	Placid gaze, serious, dispassionate; No desire for sleep or food; Scant sweat, urine, feces; Lotus-blossom face	Suspiciousness, delusion, hallucination
Guru, Vrddha, etc.	Teachers, elders, and respected ones	Bathing, purity; Solitude Versed in scriptures and poetry	Behaviour, diet, and speech indicates a curse	Auditory hallucination "by curse"
Pitr	Deceased ancestors	Devoted to mother, father, teachers, elders	Dull gaze, undiscerning; Excessive sleeping; Eats inedible substances Poor appetite and indigestion	Visual hallucination
Gandharva	Celestial musicians; associated with <i>soma</i> , love, gambling in Vedic period	Likes singing, music, someone else's wife, garlands, pleasant fragrances	Passionate, impetuous, serious; Fond of music, dance, food and drink; Red clothes; Derides ritual	Touched (by Gandharva)
Yaksa	May be divine or demonic; ruins offerings to Ancestors	Intelligent, strong, handsome; Likes humor, talks much	Sleeping, crying, laughing Fond of dance	Taken by Yaksa; Experience of being possessed
Brahma-raksasa	Ghost of unholy Brahman	Dislikes scriptures, austerities, discipline; Either a fallen Brahman or claiming high status; frolics in temple waters	Dances and laughs loudly; Hates gods, sages, and physicians; May injure himself	Unspecified
Raksasa	Evil demon with sharp teeth; ruins ancestral rites	Lacking mental clarity; Slandorous and lusting for women; Deceitful and unpleasant; Drinks and eats much	Disturbed sleep, averse to food; Fond of knives, meat, blood; Threatening	Smell of raw flesh
Pisaca	Most evil and demonic; Lurks in deserted houses, by waters, roads and trees	Lacking mental clarity, slanderous; Lusting for women; Deceitful, a braggart, hurts others	Abnormal thinking; Behaves improperly; Dancing, singing, laughing, chattering; Sleeps in filth; Nudity, running about aimlessly; Memory loss	Experience of being possessed: "They mount his back making him see"



deities that are well-known within the culture. Sushruta explains:<sup>3</sup>

They do not consort with men, nor do they  
ever take possession of men;  
And those who say that they do take  
possession are to be disregarded, since  
that kind of knowledge about the Bhutas  
is pure delusion.  
(6.60.21)

Bhutas refer to the supernatural beings that are responsible for certain kinds of disorders that originally came under the heading of Bhuta Vidya among the eight branches of Ayurveda. *Charaka Samhita*, which commands the most respect of all the texts, and *Bhela Samhita*, unlike the others, place mental disorders associated with the Bhutas in the same chapter as mental disorders caused by humoral imbalance, the Doshas.

Whether possession should be understood as the cause of the condition or just metaphorical, treatment for it indicates respect for the potency of complementary medicine and ritual. In fact, the texts appear to remain so respectful of these seemingly contradictory approaches that some scholars see in it a frustrating ambivalence towards rationalism and mysticism. The passage that follows is probably like those that Debiprasad Chattopadhyaya<sup>12</sup> had in mind when he explained that "the medical compilation [that] reaches us is full of alien propositions ... to be viewed as extrinsic to medicine, loosely inserted into the medical work" (p. 424). The following passage from *Charaka Samhita* outlines the treatment for the exogenous form of mental illness:<sup>2</sup>

With food offerings, charms, ablations, and  
possession of medicinal herbs and drugs,  
With honesty, good conduct, austerities,  
wisdom, generosity, disciplines, and  
vows  
And by honoring gods, cows, Brahmans,  
and teachers,  
The exogenous type attains tranquility-  
also with supernormal powers, sacred  
formulas, and medicinal herbs.  
(6.9.93-94)  
In a similar vein, *Sushruta Samhita* advises

a sacrifice in a particular place according to the particular spirit (e.g., in the empty house of a Pisaca, to the Pitrs at the river, and in the fire for the Devas) (6.60.32-37).<sup>3</sup> Retention of the term Bhuta Vidya as the heading for disorders like Unmada and Apasmara (epilepsy), which the texts discussed with reference to standard medical theory, may also represent a contradiction, referring to an earlier stage of medical science when thinking about these disorders was closer to magico-religious ideas of the Veda.

To whatever extent there was a transformation away from thinking about possession within the medical system, it probably had little influence on popular ideas about mental disorder and the other diseases associated with possession. Perhaps it was to some extent because of such a difference in the professional and popular understanding of Unmada that people consulted Ayurveda less for this problem than others. Other magico-religious healers may have been understood as more knowledgeable in treating the locally perceived causes of these disorders. Ethnographic field research, discussed below, suggests as much.<sup>39 40</sup>

Although the later texts say less about this branch of medicine, sometimes quoting passages from the earlier authorities verbatim, the number of spirits to which they refer in their discussion of Bhuta Vidya increases. For example, *Sarngadhara Samhita* (1.7.38-39) refers to 20, and *Astanga Samgraha* (6.7.2) specifies 16 categories of spirits associated with Unmada.<sup>38</sup> Some present-day practitioners of Ayurveda advocating more integration with allopathy appear somewhat embarrassed by the incorporation of the magico-religious into the medical tradition. Some try to explain away these supernatural beings (Bhuta), suggesting that they should in fact be understood as microorganisms. A chapter by Gaur (p. 370) on Agada Tantra and Bhuta Vidya reflects this view.<sup>11</sup>

### Ethnographic, Textual, and Clinical Studies of Ayurveda and Mental Illness

Research on Ayurveda with a focus on mental illness has been limited. Bhattacharyya



completed an ethnographic study of Pagalami, a Bengali term for severe mental disorder, in villages of West Bengal, identifying local categories and meanings of mental illness.<sup>39</sup> In the course of her work she tried unsuccessfully to locate an actively practicing Ayurvedic psychiatric specialist in or around the region of Calcutta. Although several said that they would treat such patients, they explained that these patients did not come to them. In her report, she emphasized striking discrepancies between the classical texts and current practice:<sup>39</sup>

Psychogenic factors which were ignored in Charaka and Sushruta are now emphasized and integrated into the Tridosha theory. Second, despite the resurgence and professionalization of Ayurveda in the early 1900s, facilities and personnel for the Ayurvedic treatment of mental illness are almost nonexistent. (pp. 41-42)

Although she found nowhere near the level of use of professional Ayurvedic treatment for mental disorders, she acknowledged that Ayurvedic concepts nevertheless shaped popular perceptions of illness. Her interviews with people seeking psychiatric treatment for Pagalami indicated these ideas were prominent among one of the three main popular categories of mental disorder, which included possession, sorcery, and "bad head" (Mathra golamala). The last of these is associated with a humoral imbalance, which some even called Unmada.

Blackford studied illness beliefs and psychotherapy in Banaras, interviewing patients and their families in the psychiatry outpatient department of Banaras Hindu University and six healers in the region who treat people with problems likely to be considered psychopathology by mental health professionals.<sup>40</sup> His findings showed that explanations of severe mental disorder from laypersons and the healers both described these disorders as Unmada or Pagal Pan. Most of these were attributed to possession by spirits, described as Bhutas and Prets.

My own research has included studies in several psychiatric settings in India-including work with collaborators at NIMHANS - that identified influences of Ayurveda on mental

illness.<sup>41 42</sup> An analysis of chapters of the Ayurvedic texts dealing with Unmada and Bhuta Vidya translated, analyzed, and compared the textual accounts of the categories and subcategories of these disorders.<sup>38</sup>

Journal articles, two dissertations, and a book by Gupta have studied concepts of mental disorder and psychopathology from analysis of the Sanskrit texts. Haldipur's analysis of the concept of insanity according to Charaka<sup>43</sup> is appropriately skeptical of Dube's efforts<sup>44</sup> to equate Ayurvedic to ICD categories, although his earlier paper analyzing the nosology and taxonomy of psychiatric disorders in Sushruta accepted the premise uncritically.<sup>45</sup>

Deb Sikdar in an earlier review of psychiatric disorders in the Ayurvedic texts recognized the insight of the clinicians who produced the texts.<sup>46</sup> He also found in the humoral theory the germ of modern theories of personality and body type. In addition, he concluded that the humoral theory was not just a matter of historical interest, but that it might also clarify biochemical correlates of mental disorders in the blood, bile and urine.

Gupta's *Psychopathology in Indian Medicine (Ayurveda)* is an especially wide ranging, but not necessarily clearly focused, study.<sup>47</sup> It considers the philosophical underpinnings of Ayurveda, the nature and location of mind, structure of the nervous system, and the categories and formation of personality. He completes this analysis as a preliminary to a discussion of psychopathology; Gupta distinguishes diseases with primarily mental origin and mental symptoms (Unmada); disorders with primarily mental origin and physical symptoms, epilepsy (Apasmara); physical origin and mental symptoms, intoxication (Mada); and physical origin and physical symptoms, fainting (Murcha). This analysis draws upon various sources to support the rationale, not just the Ayurvedic texts but also works in Western developmental psychology, psychoanalysis, and physiology. Although the logic of the classification is appealing, it appears to be more imposed on than following from accounts in the classical texts of Ayurveda.

Like Gupta's work, the doctoral thesis of Shukla, which was completed under the tutelage of O.N. Srivastava at Banaras Hindu University (BHU), also reviews the principle



categories of mental disorder, focusing mainly on Unmada.<sup>48</sup> His account is illustrated with the photographs of patients he interviewed with these conditions. This introduction of the principles is intended mainly to serve as background and a conceptual framework for two separate studies, an epidemiological field study and a therapeutic trial.

The mental morbidity survey, which made diagnoses based on allopathic and Ayurvedic categories, was undertaken in Sundarpur village, 2 kilometers from BHU. The survey randomly selected 1,029 individuals from the total population of 3,000. Interviews were conducted with members of the family of selected persons and also with village elders, Panwalas, shopkeepers, and others who might be able to give information the family was reluctant to provide. Diagnoses according to Western and Ayurvedic criteria were made from interview findings.

The author's analysis was based on the premise that Unmada was equivalent to any allopathic diagnosis of psychosis, which in effect reconceptualized Unmada as a translation for psychosis. Results were compared with findings from other psychiatric epidemiological studies in India. The prevalence of Unmada was found to be 12.63 per 1,000 of population, and if only adults were included in the denominator, 17.85 per 1,000. In addition to the field survey, Shukla made clinical observations on 314 outpatients and inpatients at BHU, 133 with non-psychotic illnesses and 181 patients with psychotic illnesses, which he also regarded to be Unmada.

His study also examined the constitution of patients according to Kretschmer's criteria and Ayurvedic criteria. The Ayurvedic criteria were made according to body type (wind, bile, and phlegm) and mental type, according to the three parameters of mental functioning based on the classification from the three Gunas (namely, Satva, clarity; Rajas, passion; and Tamas, lethargy). Of the 181 patients with Unmada, 49.2 percent were of the Vata type, 20.4 percent Pitta type, and 30.4 percent Kapha type. The Vata type, however, was found in very few of the 28 with a diagnosis of affective disorder, only 3.6 percent. With respect to the mental constitut-

by Satva, 46.4 percent by Rajas, and 14.9 percent by Tamas.

The concluding phase of Shukla's impressive dissertation research included a therapeutic trial with 181 patients with Unmada, comparing Shankhapushpi, an Ayurvedic drug; Jatamansi, another Ayurvedic drug; a mixture of 12 Ayurvedic drugs, termed Medhya Kashaya; allopathic treatment with neuroleptics or a tricyclic; and a placebo group. The first four showed a significantly better response than the placebo, and the group treated with Medhya Kashaya had the best response, slightly better than the allopathic treatment group, which was the next most effective. Groups 1 and 2 were each only slightly better than placebo.

As a nonblind study that did not specify inclusion criteria, the specific regimen of all treatment groups, and outcome measures to standards of a present-day clinical drug trial, the study was flawed. Nevertheless, it and comparable studies of Ayurvedic interventions raise questions requiring attention about the possibility of contributions from Ayurveda to allopathic treatment in psychiatry. In discussing Shukla's work, it is not the aim to draw any conclusions about the drugs he tested, but rather to clarify the context of such research and consider the interactions between textual, epidemiological, and clinical perspectives. Research and clinical experience in the Ayurvedic Unit at NIMHANS since its establishment in 1963 to the present makes it better able to provide a more authoritative review of the current status of Ayurvedic treatment in psychiatry.

### **Conclusion: Comparing Nosologies and Illnesses**

The development of criterion-based diagnostic systems, beginning with DSM-III, over the past two decades has focused attention within the field of psychiatry on questions of nosology to a greater extent than ever before. The opportunity to compare independently derived diagnostic systems from cultural and historical studies of Ayurveda raises important questions about the validity of such comparisons because the premises of each of the systems are so



different, even though they share similar concerns about the welfare of their patients.

Appreciation of the cultural context of psychiatric practice calls into question such efforts to equate categories of one system to those of the other. Translation from DSM to ICD is difficult enough, but doable. The effort to equate subtypes of Nija-Unmada to subtypes of schizophrenia is fraught with problems, however, because it ultimately decontextualizes both. Such equations as "Unmada is schizophrenia" or vice versa are at best simplistic, and may be meaningless and misleading, obscuring the meaning each set of terms has for patients, practitioners, and clinical care settings.

Cross-cultural comparisons of psychiatric diagnoses in Ayurveda and allopathy have been notorious in their failure to take the complexity of the vastly different contexts of the three nosologies into account. Failure to appreciate the ethnomedical aspects of DSM and ICD in their relationship to Ayurveda, and a misplaced emphasis on equating diagnostic categories have been serious shortcomings. We should not compare diagnoses without comparing diagnostic systems, and this requires serious attention to their social, cultural, and historical underpinnings.

The texts (i.e., treatises of Ayurveda, DSM, and ICD) provide accounts of illness categories, which collectively comprise each of these diagnostic systems. Since a formal system is usually only an approximation of practice, however, another step is needed for the richer account that social research and clinically meaningful comparisons require. We must expand the database for such comparisons by including the clinical experience of our colleagues, findings from studies of illness experience, and relevant social, cultural, and historical research. With that in mind, we can better appreciate the remarkable contributions of the physicians who developed the Ayurvedic concepts of mental illness, and allopathic psychiatry is likely to benefit from insights another perspective offers.

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"In order to understand what such a book is all about it is imperative to cast off certain prejudices of the Western mind... Our science is based upon the principle of causality, and causality is considered to be an axiomatic truth. But a great change in our standpoint is setting in. What Kant's 'Critique of Pure Reason' failed to do, is being accomplished by modern physics. The axioms of causality are being shaken to their foundations: we know now that what we term natural laws are merely statistical truths and thus must necessarily allow for exceptions... I am now in my eighth decade, and the changing opinions of men scarcely impress me any more; the thoughts of the old masters are of greater value to me than the philosophical prejudices of the Western mind. Unexpected cures may arise from questionable therapies and unexpected failures may arise from allegedly reliable method"..

Carl G. Jung



# Traditional Medicine/Traditions of Medicine: The Meanings of Health on Two Sides of the Globe

R. A. Shweder

## Hazards of Cross-Cultural Communication

In India, it is widely believed that the mouse is afraid of the Elephant God Ganesh, while in the United States, it is the elephant who is thought to be terrified of mice. In India, at least among rural Hindus, the owl is believed to be an inauspicious bird, an unkempt predator that viciously slaughters the crows who bear the spirits of one's ancestors during the Sraddha (love and affection) ceremony; and it is a curse to tell a married woman that she will be "reborn as an owl," while in the United States, the owl is admired for its wisdom, as if it were a sage. In the United States it is polite to say to a postpartum mother nursing a child, "what a beautiful child that is," while in India that particular remark, which Americans consider so salutary and beneficent, is used by Kalasis and Devi Sadhaks and other mediums of the Great Goddess of Hinduism to diagnose sorcery and the evil eye, and that comment, which Americans consider so innocent, is believed to cause fever, diarrhea, and vomiting in infants.

In India, even the most enlightened of medical scientists will tell you that "religion is observed for better health," while in the United States, at least among the enlightened, the very idea of religion is opposed to the idea of science and medicine, and such notions as Atma, Preta, and Chuaan (soul, ghost, ritual pollution) are associated with darkness, superstition, irrationality, and a premodern cast of mind. One of the surest ways to bring a dinner party to a halt in Manhattan or Bethesda, Maryland, is to speak earnestly about the soul or to use the word God.

In the United States, the current historical age is sometimes dubbed the "age of reason." Contemporary Americans tend to "officially"

believe (their politicians and scientists certainly talk this way) that technological progress abounds in their country and that because of their physical and biological sciences, Americans are about to seize control of nature and become the most advanced and knowledgeable human beings who have ever lived.

In India, the age of truth (Satya Yuga) is thought to have existed long ago, and the stories of the old time (the Puranas and the Epics) are the preferred standard for judging our contemporary decline into an age of darkness, which is known as Kali Yuga. With a sense of loss and with Kali Yuga very much on his mind, a brilliant Oriya Indian friend once told me:

There is nothing on the outside called God. God is within us. The human body is the only real sacred ground, and it becomes desanctified after pollution. If your lifespan is 50 years, it will decrease if you allow your body to become polluted. But if you obey every duty and custom, you will be free of pollution and you will be healthy. Nowadays, if someone suffers from fever or illness, they may be prone to say that they suffer from an infection. They do not believe in pollution and the other causes. It has long ago been written that during the days of Kali Yuga, people will abandon their traditions and only think this way.

I mention these striking contrasts between India and the United States because this is an Indo-U.S.A. Workshop on "Traditional Medicine and Mental Health." Yet every one of the words in that title, with the possible exception of the "and" is likely to connote a somewhat different set of meanings on each side of the hyphen in the phrase "Indo-U.S.A."



I mention those differences in the meaning of things in our two lands because the metaphysical jet lag of a long journey in either direction between India and the United States is likely to be far more severe than the mere physical jet lag. I mention them because the ingestion of melatonin will not work as a cure for the subtle misunderstandings that are likely to arise when words such as traditional, medicine, mental, and health get used as though we really shared a common language. In fact, such words evoke somewhat different pictures of the world in the minds of speakers from different intellectual traditions.

For example, years ago when I first started doing research in the temple town of Bhubaneswar in Orissa, India, my Oriya colleagues would sometimes say to me "She is a very shy girl" as a way of recommending a student as a research assistant. What they did not realize was that that is definitely not the way to recommend someone for a job (or for anything else) in the United States. In the United States, the English word "shy" implies meekness, timidity, insecurity, and weakness (not to mention such culture-specific metaphors as sheepish and mousy).

What I did not realize at the time, at least initially, was that bilingual Oriya-English speakers use the English word shy as a translation of the Oriya word *lajya*. There really is no adequate single lexical translation in American English for *lajya*, although the paraphrase "a civilized person who displays the emotion and virtue of respectful restraint" captures its meaning far better than the word shy. During the Victorian period in England, the novelist Jane Austen knew all about the concept of *lajya* or respectful restraint, but it is a relatively dormant and unacknowledged emotion and virtue in the United States today. So when my Oriya colleagues said, "You should hire her; she is a very shy girl" I did not understand that in their minds the word shy (as the translation of *lajya*) was meant to imply unpretentious, not brazen, having humility, self-restrained, elegant, decent and good.<sup>12</sup> I discovered in the case of "she is a shy girl" that to use the same words is not necessarily to speak the same language. I discovered that if you really want to learn about other peoples' meaning for things, it is essential to be aware that the

appearance of shared understanding can be an illusion.

### **Traditional Medicine Compared to What?**

I suspect the same problem of hazardous cross-cultural translation and communication will arise in our discussions of traditional medicine and mental health. On each side of the hyphen in Indo-U.S.A., some apparently transparent English word (health, medicine, mental, traditional) will be associated with a somewhat different picture of the domain to which each of us thinks the word is meant to refer. Consider, for example, the phrase traditional medicine. In the context of the two major Western intellectual traditions with which I am most familiar, enlightenment modernism and counter-enlightenment romanticism,<sup>3</sup> the phrase traditional medicine almost inevitably suggests some kind of contrast or opposition between modern medicine (equated with Western allopathic medicine) and traditional medicine (equated with everything else), typically to the denigration of one or the other.

There are of course many intellectual crosscurrents in the United States today, just as there are in India. Nevertheless, in most of the discourse on this topic, the label traditional medicine gets used as a way of contrasting Western allopathic representations of biological disease processes to something else (indeed to anything else). The "anything else" is called traditional medicine (although the phrase alternative medicine is also now coming into vogue, due in large part to efforts at the National Institutes of Health-NIH). Thus, within the United States, the phrase traditional medicine often takes on the meaning "health doctrines and practices which are not contemporary Western allopathic medicine." The phrase then gets used to refer to a vast and heterogeneous collection of theories and therapies, ranging all the way from alternative representations of the biological causes of suffering (e.g., Ayurvedic theories about the Doshas or humors of the body) to various forms of Christian charismatic spiritual healing.



Among enlightenment modernists, that particular scheme of interpretation (modern=Western allopathic medicine, traditional=everything else) plays itself out as follows. Western allopathic medicine is said to be modern, not traditional. A series of oppositions is then invoked in which it is claimed that the traditional is to the modern as darkness is to light, as superstition is to knowledge, as backward obsolescence is to the advanced cutting edge, and so forth. Thus, at least among enlightened modernists in the United States, the label traditional medicine gets used as a code word for pseudo-healers who are charlatans and quacks, in contrast to modern healers who are supposed to have transcended tradition and thereby gained objective access to the truth. (Parenthetically, it is important to note that most enlightenment modernists do allow that at least some so-called traditional medicine has been mislabeled and that at least some it is really modern medicine in disguise. Consequently, most enlightenment modernists are open to the possibility that at least some so-called traditional healers are effective healers, although they believe such healers are effective because they are actually practicing modern medicine, albeit unknowingly and without a license.) Consider, for example, the Kalasi in a local temple in Orissa, who is a medium of the Goddess and specializes in the diagnosis and treatment of young children's ailments. At least some of my enlightenment modernist friends are impressed by his covertly modern and up-to-date medical prescriptions to mothers of sick infants.

The following is from a transcript of a healing session collected by a former student of mine, Kathleen Chattin, in connection with our research on the moral basis of family life practice in Bhubaneswar. Notice that from an enlightened modernist perspective, the Kalasi seems to give some shrewd medical advice to his client, involving hygiene and the use of rehydration fluids and electrolytes. (The Kalasi's yawns are an indication that he is possessed by the Goddess and speaks on her behalf.)

Kalasi: What is the name of the child?

Mother: M.

(The Kalasi yawns.)

Kalasi: Keep the Paduka (the flowers offered to the Goddess) on the bed of the child where he would rest his head.

Mother: The child has diarrhea and vomiting.

Kalasi: What happened?

Mother: He has diarrhea. His stool has mucus in it. He vomits.

Kalasi: What is his name?

Mother: M.

(The Kalasi yawns and there is a tapping sound made with the sticks he uses to treat the evil eye and exorcise spirits.)

Kalasi: Are you breastfeeding him? Does he strain when defecating?

Mother: Yes.

Kalasi: What about his diet?

Mother: Barley.

Kalasi: Boil barley and sugar. Then cool down the stuff. Add some portion of the enchanted salt to the stuff and feed that to the baby. Do not touch the salt without taking a bath. The next evening you will inform me about the developments.

So enlightenment modernists are not always disparaging of so-called traditional medicine because they readily grant that some so-called traditional medicine is more modern than we realize. Moreover, enlightenment modernists can be quite entrepreneurial about the chemistry and salubrious properties of the roots and shoots of the jungle. There are private companies in the United States (for example, Shaman Pharmaceuticals, Inc.) who are well aware that approximately 150 drugs (digitalis, quinine) have been synthesized from the medicinal barks, roots, and leaves of so-called traditional healers. These companies invest heavily in the acquisition and laboratory analysis of the natural substances utilized by so-called traditional healers around the world. Their aim is to isolate component chemicals and then license them with the FDA (Food and Drug Administration of the U.S. Government), thereby upgrading the status of so-called traditional therapies by officially certifying them as "modern medicine." It is noteworthy that neither Shaman Pharmaceuticals Inc. nor the FDA invests in placebo cures.

Although enlightenment modernism is a



strong voice in the West, another voice can also be heard in the United States these days, the voice of counter-enlightenment romanticism. When it comes to the contrast between traditional medicine and modern medicine, counter-enlightenment romantics typically reverse the direction of darkness versus light. Counter-enlightenment romantics are there-by, in the context of contemporary scientific and political debates in the United States, always vulnerable to the accusation of being "soft on superstition." For counter-enlightenment romantics, the very idea of traditional medicine suggests something old, venerable, good, and useful, and it does so precisely because traditional medicine is seen as an alternative to so-called modern medicine. Guided by the lights of tradition, counter-enlightenment romantics hope to recapture what modern medicine has lost, a mature understanding of the mental side of somatic experience and of the whole person as a psychological, social, and political being. Counter-enlightenment romantics hope to resist the specific version of biological representation and therapeutic practice (e.g., the reductive idea of autonomous biological disease processes, excessively potent synthetic drugs, invasive surgery) associated with mainstream biomedicine in the West. Notice, however, that both intellectual traditions (enlightenment modernism and counter-enlightenment romanticism) presuppose mainstream medicine as currently institutionalized and empowered in the West as the reference point for defining what counts as traditional. For both camps, the very idea of traditional medicine is defined by contrast to the contemporary Western mainstream. For better or worse, this seems like a rather ironical and parochial way of defining one's terms -where the only way to be modern is to be part of the mainstream, and the only mainstream that counts is the one that runs through the West.

### **From Traditional Medicine To Traditions of Medicine**

One of my aims today in the context of an international meeting held in Bangalore rather than in Boston is to shake myself free

of this type of thinking. During the years I have spent documenting and writing about family life and social practices in India, I have learned many things from some of the doctrines, customs, and habits of mind that have grown up or thrived on the subcontinent of Bharat. One of the things I have learned is that in South Asia (more specifically, in rural India; even more specifically in rural Orissa, India), there is no special privilege accorded to Western allopathic medicine. In the region of India in which I work, Western (allopathic) medicine is highly respected for its treatment of certain kinds of ailments in adults, but it is respected as only one worthy tradition of medicine among many.

To anyone familiar with the South Asian cultural scene this should come as no surprise. Given the contemporary and quite luxurious metaphysics subscribed to by hundreds of millions of Hindus in rural India, when suffering occurs the diagnostic situation is understandably quite complex. For one thing, there is not just one world to deal with but three: the society of the gods (who are a major presence in almost every household and community), the society of the spirits (Preta Loka and Pitru Loka, who are also a major presence in almost every household and community), and the society of human beings.

Secondly, these three worlds all interact in a universe governed by the principles of Dharma (truth, righteousness, duty) and the laws of Karma (the idea that for every action there is a just or proportionate reaction; it is natural, moral, and inevitable to reap what you sow). Thus for any physical or mental difficulty, there are very many possible causes. The difficulty might be caused by an infection, by a disruption of the humoral (Dosha) content of the body, by a Karmic debt related to some transgression of duty in this and earlier lives, by a pollution of one's sacred body, or by the unwelcome, even if temporary, influence of one of the nine malevolent planets. The difficulty might be caused by a curse from an envious neighbor or by the influence of some evil spirit. Perhaps a Chandi (some unworshipped goddess) or a Bhuta (the ghost of someone whose cremation process went away) or a Chiriguni, Pichasuni, or Brahmarakyas (in each case, the lingering



and discontent spirit of someone, a pregnant woman, a Brahman, who died suddenly, scandalously, or without satisfaction of his or her desires) has been sent by a Guni or tantric magician to harm you, to attack your somatic or mental functions, or to invade your body and take over or confuse your will.

Moreover, given this complex yet compelling picture of the potential causal forces of nature, the domain of potentially plausible healers grows very large. It includes allopathic doctors, homeopaths, Brahman priests, Baidya, Kabirajs and other Ayurvedic doctors, Kalasis (devoted mediums of the Goddess), Ojhas (astrologers), Poothis (oracular consultants of palm leaf manuscripts who can identify your transgressions in past lives), Devi Sadhaks (agents of the Goddess who are able to diagnose the true causes of illness by means of Pranayama -meditative breathing), and many others.

The range of potentially plausible therapies is equally diverse. It includes antibiotics, herbal medicines, Satvika (pious boiled) foods, the consumption of the sun-dried rice or Nimalya that is the Prasad (the uneaten remains of the food offered to a God) of Juggernaut or Vishnu, the ingestion or application to the body of the five products of the cow (ghee, curds, urine, dung, milk), the recitation of Mantras, the reading of scriptures, the singing of Kirtans (musical prayers), the offering of food (Bhoga) to gods and ancestors, the exorcism of invading spirits, animal sacrifice, selfabnegation and devotional pilgrimage, the use of talismans, rubdowns of turmeric, the feeding of Brahmans, Paduka (the medicinal use of flowers offered to the Goddess and of the water used to wash her feet), ritual cleansings, Yoga, breathing exercises, and a highly significant dose of optimism and faith.

Moreover, these various traditions of medicine are not inherently opposed. Most rural folk and healers in rural India share with each other the following kinds of beliefs:

- Some illnesses are caused by infections of the body, and many are not.
- There are numerous pains and aches of the body -of the head, the chest, the legs, and the back-for which doctors have no

- Diarrhea and the painful feeling that your body is being pierced by a needle can have many possible causes.
- Powerful 'black magicians' can make you lose weight or disrupt your digestion and have the capacity to paralyze you, make you behave strangely and shamelessly, and may even be able to drive you mad.
- Urine, stool, semen, blood, and other fluids of the body can be used as diagnostic signs of some of the true cause of suffering--both biological and spiritual.
- When the medicine of the allopath and the baidya (ayurvedic) do not work, you should consider going to a Kalasi.
- When neither the doctor at the hospital nor the Goddess in the temple is able to cure you, something else must be going on.
- The society of spirits exists, and spirits have the ability to trouble human beings.
- Demonic planets can influence the Doshas of the body (for example, producing an excess of black bile).
- Ayurvedic doctors are not very well versed in childhood illnesses.
- To be envious of others or covetous of their possessions is to automatically cast an evil eye.
- The experience of the emotion of fear (and psychological weakness more generally) is the major prelude to the harmful effects of evil eye and spirit possession.
- When fear is the cause of suffering, allopathic and homeopathic doctors can do nothing about it, but one may be cured with talismans or by an exorcism.
- Some children are fearless and thus have a natural immunity to evil eye.
- There is a difference between a case of mental illness and a case of spirit possession.
- If you get no results from exorcism, then evil eye is not at work in that instance.
- Ritual purity and righteous behavior protect you from sorcery and disease.
- Some illnesses are cured very quickly with allopathic medicines, and Ayurvedic remedies are more gentle and gradual and take a longer time.
- Quacks, charlatans, pretenders, fakes, and incompetents exist within every tradition of healing.



- Protective devices such as talismans may be rendered useless by the pollutions emanating from death, birth, and menstrual blood.
- There is an appropriate food for every occasion and an appropriate substance that you can ingest for almost any difficulty: boiled barley with sugar and salt added can be good for infant diarrhea; boiled fresh ghee with an egg and some ginger added is good for a common cold.
- Eating a lot of "hot" foods may delay menopause for several years, which is not something any rational person would want to do.
- The body is made of the five basic elements, in particular, air, water, fire, earth, and ether.
- There are six Chakras and ten Indriyas (gates or openings to the body, for example, the two eyes, the two ears, the anus, the genitals, etc.).
- Too much sex is bad for your health and is especially bad for you on the Sankranti day (new moon day) and the Ekadasi day (11th day of the new moon cycle).
- Many aspects of your fate are written on your forehead in the first few days after your birth as just dessert for your virtuous and vicious actions in previous lives.
- Old sins and spiritual debts cast long shadows and thus ultimately the past catches up, even across rebirths.
- When it comes to understanding the complex causal forces and interactions of the human, spiritual, and divine worlds as they relate to any particular instance of illness and suffering, mere mortals are bound to be as ignorant as they are knowledgeable.

Because these ideas and understandings are widely shared in rural India, it should come as no surprise that after diagnosing your symptoms, the doctor in the local hospital may send you to a Kalasi, or that after reading your signs, the Kalasi (the medium of the Goddess at the local temple) may send you either to a devi Sadhak (someone capable of doing battle with the evil spirit sent by a powerful sorcerer) or to an eye doctor. Thus, one lesson I have learned in India is that it makes far more sense to speak

of traditions of medicine rather than of traditional medicine, while recognizing that every tradition of medicine, including Western allopathic medicine, is a historical entity that has its own ancient and contemporary forms. No tradition of medicine is uniquely modern. When someone asks you to speak about traditional medicine, the most appropriate reply is, "Which tradition of medicine?" Or put the other way around, of the many traditions of medicine, why should we say that only this one or that one is traditional?

In the remainder of this essay, I attempt to quickly canvas the broad domain called health and to elucidate some of the many traditions of medicine that exist and persist on a worldwide scale and in India as well. As far as I can tell, almost every mode of medical thought and practice that has ever existed anywhere in the world (from Plato's ideas about reincarnating souls to Galen's biological theory of the humors of the body) has either been independently invented in India or has migrated to the subcontinent and flourished there and continues to be carried forward and advanced by some tradition of healing or another. I want to suggest that there are many traditions of medicine precisely because there is something essentially contestable about the very idea of health and about the orders of reality that might plausibly be invoked in any particular explanation of suffering.

### **The Many Meanings of Health in One City in the United States**

The most common way to conduct research on health in the United States is not through a physical examination or through the analysis of blood and urine or other juices, fibers, or organs of the body. The most common way is through survey research in which respondents are asked questions, and the most common question asked is this one: "How would you rate your overall health (excellent, very good, good, fair, poor)?" No one is quite sure what that question means, although people who say they are in poor health seem to die sooner than people who say they are in excellent health, and the answer to the question predicts mortality



somewhat better than laboratory results and a physical examination by a doctor.

A few years ago, I conducted a graduate seminar at the University of Chicago on "Culture and Health" in which we attempted to determine what images and meanings members of seven different ethnic groups in the city of Chicago associate with the English word health when they are asked to answer that apparently straightforward, simple, and predictively powerful survey probe. The members of the seminar conducted in-depth interviews with a small sample of Polish-Americans, African-Americans, German-Americans, Hispanics, Haitians, Japanese-Americans, and Chinese-Americans. Among other things, we asked our informants to answer the question, "How would you rate your overall health (excellent, very good, good, fair, poor)?" We then asked them to tell us what they thought we meant by the word health when we asked the question. What we discovered was that "health" indexes a wide variety of intuitions, images, and meanings about personal wellbeing.<sup>4</sup> It activates somewhat different pictures of personal wellbeing for different respondents and is not a unitary concept. Here are some of the diverse intuitions, images, and meanings of health that we uncovered.

- Health as energy, as energy reserve, or as energy potential. The basic idea here is that illness is the loss of your energy reserve or potentiality, and when that happens, as one informant put it, "you make a fast step to the bottom."
- Health as the absence of unpleasant symptoms, including aches, pain, and fever. The basic idea here is that you are healthy whenever the biological functioning of your body does not intrude itself into your consciousness, or as one informant put it, "nothing hurts, nothing itches."
- Health as the ability to carry on the functions, duties, and activities of everyday life. The basic idea here is that illness is the disruption of your capacity to perform your daily routines or, as one informant put it, to be healthy is "being able to get around and enjoy yourself."

- One fascinating variation on this

functional idea of health is health as autonomy. The basic idea here is that health means being able to function without a dependence on drugs, technologies, special assistants, or anyone else. In other words, if you require eye glasses to see, then you are less healthy. If you have to use insulin to keep your blood sugar level under control, then you are less healthy. If you need to have your children around to keep you from feeling sad and lonely, then you are less healthy, and so forth.

- Health as an objective physical fitness standard. For some informants, health meant being able to engage in some strenuous exercise; for example, they might rate their health on the basis of the number of miles they could run each day. Health might mean 10 miles a day. For other informants, especially for some of the women in our sample, weight and waist line were significant aspects of their conception of well-being. The basic idea here is that you fall short of being healthy if you can't live up to some objective standard which defines being physically fit.
  - One fascinating variant on this objective physical fitness standard idea of health that is now taking hold in the United States, perhaps under the dual influence of insurance companies and epidemiological researchers, is health as an absence of statistical risk factors. The basic idea here is that you are unhealthy or sick not because you are actually suffering but because you have some of the risk factors (overweight, smokes, no physical exercise, fatty diet) statistically associated with suffering in the general population. According to this idea of health, you do not have to suffer to be perceived as sick. You just have to be difficult to insure. In the minds of some Americans, the risk factors associated with illness have become the disease.
- Health as diet or food. The basic idea here is that the nature of the substances ingested into your body is the cause, expression, and indicator of your overall well-being. The idea is that you keep yourself



- and your family healthy by eating the right foods; it is not possible to be thought of as healthy, elevated, or good if you who eat the wrong kinds of foods.
- Health as the hardiness or the purity of one's inherited stock. The basic idea here is that to be healthy is to be able to resist and not succumb to all the bad or evil forces in the world (germs, viruses, etc.). One's capacity to flourish in the face of all the dark forces of suffering can be traced to either good genes, a powerful immunological system or some other ennobling characteristic of your biological lineage.
- Health as freedom from disease. The basic idea here is that health is a state of purity characterizing your body, your mind, and your immediate social and physical world. Sickness is a state of contamination or pollution of psyche, soma, and environment by the destructive forces (germs, negative emotions, bad thoughts) that might make you suffer.
- Health as a fragile equilibrium, a balance among diseases. Some people think of the human body as inherently diseased, bustling with germs, packed with toxins, and highly vulnerable to suffering. From this point of view, health is a fragile state of well-being experienced when different diseases, germs, toxins, and other nasty things floating around in your veins counterbalance each other and are in equipoise. This physical equilibrium can be easily disrupted. Sickness is produced by any loss of balance or mental serenity, for example, as a result of fear, surprise, or traumatic shock.
- Health as control and management of the emotions. The basic idea here is that illness, especially mental illness, is the loss of appropriate emotional control and self-regulation of, for example, anger, fear (anxiety), and sadness; healthy people know how to interact normally and in a dignified way with others in certain core social situations. It is tempting to wonder whether this image of health has some special relevance in the context of South Asian family life, where having no sense of shame (*Lajya*) is sometimes associated with sickness, and a well-managed sense of

- respectful restraint (not shyness as described above, but sensitivity to the station and prerogatives of others) is both a constituent and a marker of personal well-being.

It is not hard to imagine how each of these intuitions about health might become the root concept for some elaborated school of medical thought. It is also not hard to imagine how each of these intuitions might already be partly informed by some well-worked-out tradition of medicine (for example, the concept of energy or chi in Chinese acupuncture) which has had an influence on popular culture in the United States. My only point in enumerating all the different ways in which the abstract idea of health can be defined and given character is to suggest that the domain of health is sufficiently complex to support many traditions of medicine, without any one of them claiming special privilege.

### **The Many Traditions of Medicine: Which Is Traditional?**

Not only is the very idea of health essentially contestable but so too are the orders of reality that might be invoked to explain why someone suffers. To suffer is to experience a devalued and unwanted state of mind, body, or spirit. In a recent manuscript,<sup>5</sup> we surveyed explanations of illness and therapeutic practices reported by anthropologists on a worldwide scale, and we summarized some of the causal ontologies or orders of reality that are held responsible for suffering by indigenous folk and healers around the world. We introduced the idea of the big three explanations of suffering, which I briefly recapitulate here.

"Everywhere in the world, people believe in spirits; it is only in India that we treat the body with Mantras." That remark, made by a local Oriya astrologer or *Ojha*, is essentially correct. There are certain very broad traditions of medicine (and associated causal ontologies of suffering and therapeutic practices) that are quite widespread around the world and other traditions of medicine that seem far more restricted in their appeal. The big three traditions of medicine are as follows:<sup>5</sup>



### **The Biomedical Tradition**

The causal ontology of this tradition is notable for its explanatory reference to the fluids, juices, fibers, and organs of the body. The therapeutic practices of this tradition focus on the ingestion of special substances (roots and shoots, chemical compounds, vegetable compounds, vitamins) and on the direct or indirect repair or removal of damaged fibers or organs.

The biomedical tradition of medicine is, of course, not peculiar to Western medicine, although critics of biomedicine in the West sometimes suggest as much. Humoral classifications of suffering, for example, are well within this biomedical tradition of medicine and are found all over the world. Humoral classifications group symptoms into kinds on the basis of their presumed psychobiological or somatic causal link to a particular fluid of a particular internal organ.

It is not hard to understand how organs and fluids can serve this taxonomic function or why such biomedical thinking is so appealing. For example, normal versus abnormal conditions of the liver (a cool liver, a splitting liver) can be used as a way of making reference to, classifying, and explaining positive (purified) versus negative (poisonous) somatic and affective feeling states. It can serve this function because of certain ideas people have about the role of the liver, for example, that it removes toxins from the blood and is a catchment for poisons. Humoral theorists in many parts of the world have spent a lot of creative energy mapping liver malfunctions and the envisioned release of toxins into one's system onto various kinds of negative emotions (e.g., irascibility) and onto various symptomatic nonemotional feeling states (e.g., an itchy skin rash).

Humoral thinking is so widespread that even among enlightenment modernists in the United States, who have long since "officially" rejected this way of thinking about human suffering, it is almost commonplace to associate emotions such as anger, fear, love, sympathy, envy, and sadness with conditions of the blood, a humor of the heart. All the following meanings are well-entrenched in American English. The blood boils = anger. The blood curdles = fear. The blood flows es to

freely because the heart pounds or because the heart breaks = love. The blood gets tired or ceases to flow because the heart is heavy or because there is a stone resting on the heart = sadness. There is no responsive blood flow because you are hard-hearted or have a heart of stone = lacking in feeling and sympathy. Because of a lack of responsive blood flow one has turned "green" = envy. Of course, not all biomedical explanations of suffering are the same. In the current mainstream Western variant of biomedical tradition, the explanatory reference is to genetic defects, hormone imbalances, organ pathologies, and physiological impairments. In the current mainstream Hindu Ayurvedic variant of the biomedical tradition the explanatory reference is to the Doshas of the body and to other constituent elements of the body. Nevertheless, it is not difficult to recognize a certain deep kinship between geneticists, biochemists, and brain scientists at NIH and researchers at Ayurvedic Institutes in India. The particular fluids, juices, fibers, and organs to which they attend may differ in the extreme, yet from a broader biomedical perspective, their discourses are but two currents in the same traditional "river of fibers and juices" explanation.

### **The Interpersonal Tradition**

The causal ontology of this tradition is notable for its references to sorcery, bewitchment, evil eye, black magic, spirit attack, and to potions and poisons of various kinds used to control others. This tradition of explanation is associated with the idea that one can be made sick by the envy or ill-will of relatives, neighbours, schoolmates, and colleagues who want you to die, suffer, fail, or fall under their influence. The therapeutic practices of this medical tradition focus on protective devices such as talismans, strategies for aggressive counterattack such as countersorcery and, quite crucially, and perhaps most importantly, on the repair of normal interpersonal relationships. The interpersonal tradition of medicine is found almost everywhere in the world, and it is well developed in India.

Kalasi: The child has been killed.

Woman: By whom?

Kalasi: A spirit has killed the baby.



Otherwise the baby was okay.

Woman: Who planned it so?

Kalasi: Could you not understand? It was an evil spirit who did this.

Woman: No. I wanted to say, was it done by any person who is our enemy?

Kalasi: No. It was nothing of that sort. It was not done by your enemy.

(The Kalasi yawns.)

Kalasi: You went to the latrine. An evil spirit was staying there. It came into your body and then spoiled the baby. That is the fact.

(The Kalasi yawns.)

Kalasi: Don't worry and bother for the dead child.

Woman: After that we have tried with various kinds of medicines [to have another baby].

Kalasi: Until now you have not gotten any result? What is your name?

Woman: K.

(The Kalasi yawns.)

Kalasi: Do you dream?

Woman: Yes. I dream different dreams. I have a lot of mental worries.

Kalasi: You must be dreaming bad dreams. It is only because of that you cannot carry a baby. Everything will be okay after you stop dreaming bad dreams.

Woman: Why [do you mention] bad dreams?

Kalasi: Bad dreams are not good.

Woman: Then what can be done?

Kalasi: This [dreaming of bad dreams] will be stopped.

Woman: I have been suffering since the baby died.

Kalasi: You regularly dream bad dreams.

(The Kalasi yawns.)

Kalasi: Would you be able to have a talisman made in gold?

Woman: I have a talisman of gold.

Kalasi: You will give that talisman to a goldsmith so it may be purified again by fire. Then you will come to me. You will bring 500 grams of ghee.

Woman: But where can I get pure ghee? These days I can only get adulterated things.

Kalasi: But try to get a good quality of ghee.

Woman: Will I not be sick again if I do as you advise?

Kalasi: You yourself will be able to feel the difference.

Woman: Okay. How about carrying a baby?

Kalasi: Yes. You will carry a baby. For that reason these things are prescribed for you. You will give birth to a male child. There is no doubt about it. But it will happen only after you stop dreaming bad dreams.

Another type of application of interpersonal medicine in rural India occurs in the context of the difficulties that sometimes arise during the female life stage known as Jouvana (which begins when a woman gets married, typically between ages 18 and 25, and ends when she becomes the manager of the household and enters the life stage of Prauda or mature adulthood, typically in her early to mid-thirties).<sup>6</sup> Customary morality in rural India encourages arranged marriage and joint family living in the extended household of the parents of the groom. At the time of marriage, a woman shifts her kinship affiliation and is adopted into the lineage of the husband. A newly wed bride enters into a social status that is widely recognized in Hindu society as a temporary but difficult and vulnerable period of life. During Jouvana, there is a major loss of autonomy, power, control, and social support. There is the pressure and responsibility to have children and at least one male offspring. From the time she is married until the next stage of life, when a woman assumes the role of household manager, a young woman in Jouvana is more or less confined to her mother-in-laws house, where she devotes herself to doing service for many of the senior relatives in her new family.<sup>6</sup> For many young newly wed women in India, Jouvana is a period of life when the respect, deference, and service they provide to the house of people who are initially strangers is rewarded by a sense of incorporation into a new kinship group and by the anticipation of the far more empowering life stage of Prauda that is yet to come. I mention Jouvana, however, because it has been reported by some scholars of Hindu family that this is the time when young women are especially prone to mental illness and to displays of listlessness, dissociative states, and other symptoms associated in the annals of Western psychiatry with hysteria.



An alternative interpretation that is widely available in rural India is that these women are not mentally ill but are rather momentarily possessed by a spirit and need to be exorcised. For example, as strange as this may seem to mental health researchers in the United States, in whose minds the society of the spirits and the society of the Gods do not exist, the following story is well within the range of imagined possibility and rational discourse among many thoughtful people in India.

There was a local Oriya man who captured two female spirits with his Mantras and did all sorts of mischief with them. The spirits were named Malli and Champa. Everyone in the community knew that he had captured these spirits and kept them in his back courtyard where they protected his mango tree so no one could pick his fruit. What this man did was send his spirits to houses where newly married brides had arrived. The spirit went there and instantly the bride was possessed. It is a matter of shame to a family if a newly married bride gets possessed and acts as though she is senseless. So some of the family members would approach this man for a cure and he would remove the spirit and charge five rupees. Sometimes he would send the spirit a second time and then remove it again and the young women would be cured. People hated him for sending spirits into their homes and they abused him when he died but they needed him to make their daughters-in-law well.

(This story, of course, presupposes the efficacy of exorcism, which is not an issue I shall address in this essay. But before we draw any strong conclusions about exorcism, we might do well to remember what some historians of 16th and 17th century Europe have pointed out, namely, that no Protestant critic of Catholic exorcism ever complained that demonic possession was a chronic condition. In Europe back in those days exorcism may have actually worked to cure Catholics of spirit attack.)

Is it possible to be possessed or confused by a spirit without being mentally ill? Is it possible for madness (Paga) not to be a mental illness? I suspect many Hindus in

rural India would say, 'Yes, of course.' I suspect most mental health researchers in the United States would say, 'Don't be ridiculous' or 'Of course not.' Most mental health researchers in the United States have a much less luxurious metaphysics than Hindus in India. Most mental health researchers in the United States are prone to infer mental illness in cases where a young woman starts acting as though this is not a pretense and there is a spirit in my body that has neutralized my will and it is really real.

The critical question that arises for this conference, however, is whether it is possible for scholars who do not share the same metaphysics or picture of what is real to agree on what the domain of mental illness is really all about. I suspect that this is once again one of those areas where-if we do not get beyond the illusion of shared meaning (she's a shy girl) we may never learn what the other conception of the mental, of the emotions, and of mental and emotional health is really all about. The best known Hindu theory of the basic emotions (the phrase basic emotions is itself a hazardous translation of the Sanskrit term *Rasa*), for example, is not closely aligned with ideas about basic emotions current in the United States.<sup>7</sup> It is not even clear that widely held American notions about mind, heart, and body (e.g., the idea that the mind is located in the head) map easily onto Hindu notions of *Atma*, *Purusa*, *Bibek*, *Budhi*, and *Mana*. Close attention to these issues is needed before we can be confident that we are speaking about the same things.

### **The Moral Tradition**

The causal ontology of this tradition is notable for its references to transgressions of obligation, omissions of duty, and ethical failures of all kinds. The basic idea behind this approach to medicine is that suffering is the result of one's own actions and intentions that outcomes (e.g., venereal disease) are proportionate to actions (e.g., sexual promiscuity) and that a loss of moral character is a prelude to misfortune and disaster. The therapeutic practices of this tradition focus on purification, confession, reparation, moral education, the adoption and continual maintenance of right practices, and



the removal of accumulated spiritual debts by means of austere denials (e.g., fasting) and even self-mortification. The health behavior movement in the United States, with its emphasis on clean living and ascetic habits ("Just say no" to fatty foods, cigarettes, alcohol, and premarital or extramarital sex) is well within this tradition of medicine.

I am not going to say very much more about the moral tradition of medicine in India in this essay, except to note a few propositions that many Hindus consider obvious or self-evident. For example, that religion, family life practice, and personal habits are closely interwoven and are not separate domains (e.g., the kitchen is a holy place, the preparation of food is a sacramental event, the eating of food is an oblation, and who eats with whom in the family is regulated by rules of ritual purity). For example, that much, perhaps most, suffering of mind and body is caused or mediated by behavior according to the laws of karma and therefore the customary morality or immorality of a group will produce well-being or suffering as its consequence. For example, that the maintenance of the purity of one's own body is a major aim in life, and a violation of customary behavior is a pollution which must be removed if one is to approach the God in the temple or even the God in your own home. For example, that religion (which includes customary practices and personal habits) is observed for better health. (See reference 5 for a detailed discussion of moral explanations of suffering, with special reference to the idea of Karma, and the collection of essays in reference 8.)

Ablutions, ablations, pilgrimages, and acts of purification of all kinds, often performed after consultation with Brahman priests and other experts on purity and pollution, are so much part and parcel of the Hindu way of life that it is easy to overlook the fact that they are highly refined applications of a moral tradition of medicine. As a result, Hindus are among the least fatalistic people I know. When things go wrong, when they have difficulties in life, when they suffer pain and anxiety, they wonder about their spiritual debts, and they believe there is always something they can do to empower themselves and improve their prospects for

the future.

Indeed, although I do not wish to overstate this point, I want to conclude with an observation about the cultural psychology of moral responsibility and personal control in India. It seems to me noteworthy and revealing of the different intellectual tempers of the United States and India that when troubled Americans consult with a therapist to "recover memories" from early childhood, they tend to recall themselves as victims and blame others for their current distress. What inference are we to draw from the contrasting fact that when troubled Hindus consult with a Poothi (an oracle) to recover information about their earlier lives, they invariably discover some fault of their own. First they are informed about some sin or transgression they committed in the distant past. Then they are given several prescriptions (make a sacrifice to the Goddess, ingest the five products of the cow) to offset their spiritual debts with some acts of virtue. In India, it is widely believed that the mouse is afraid of the Elephant God Ganesh, while in the United States it is the elephant who is thought to be terrified of mice.

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"Modern Science, obsessed with the greatness of its physical discoveries and the idea of the sole existence of Matter, has long attempted to base upon physical data even in its study of Soul and Mind and of those workings of Nature in man and animal in which a knowledge of psychology is as important as any of the physical sciences. Its very psychology founded itself upon physiology and the scrutiny of the brain and nervous system...."

"Recently, however, the all-sufficiency of Matter to explain Mind and Soul has begun to be doubted and a movement of emancipation from the obsession of physical science has set in, although it has not gone beyond a few awkward and rudimentary stumblings."

"... rationalistic and physical science has overpassed itself and before long must be overtaken by a mounting flood of psychological and psychic knowledge which cannot fail to compel quite a new view of the human being and open a new vista before mankind."

".... future in which a higher spiritual and supramental consciousness shall emerge and be turned upon the works of mind. But at present it is this which is at work; a self-conscious soul in mind, mental being- manomaya purusha - struggles to arrive at some intelligent ordering of its self and life and some indefinite, perhaps infinite development of the powers and potentialities of the human instrument.

- Sri Aurobindo



# Beyond DSM-IV: Toward a Functional Anatomy of Psychiatric Syndromes

P. Whybrow

Diagnosis in Western psychiatry is based almost entirely on phenomenology—a cross-sectional description of the syndrome—informed by longitudinal and family analysis. Although in recent decades these syndromal categories, or phenotypes, have been further defined by outcome research, including response to treatment, the fundamental classification remains similar to that laid down by Kraepelin 100 years ago.

The behaviors disturbed in psychiatric disorders, including emotion, attachment, social behavior, memory, and body homeostasis (sleeping, appetite, etc.), are functions of the old mammalian brain or limbic system. Advances in neuroscience and neuropharmacology over the past three decades have provided a functional neuro-

anatomy of this system and a general understanding of the peptide and aminergic chemistry that sustains its neural communication. More recently the advent of molecular techniques, particularly genetic analysis, promises novel opportunities in the investigation of complex mammalian behavior and an entirely new prospect for redefining the vulnerabilities that underpin the final phenotypic common pathways that we now classify as psychiatric disease.

Affective disorders can be used as a model to outline the functional anatomy of the syndrome of depression. Molecular analysis of complex behavior in small mammals will aid in redefining specific behavioral phenotypes that are disturbed in affective illness.

Depression is a complex disorder which could result from dysfunction of a number of systems... Several of the antidepressant drugs block reuptake or metabolism of 5-HT and NE. However therapeutic action of antidepressants require chronic administration. This led to the hypothesis that long adaptive changes underlie the therapeutic actions of these treatments (Heninger & Charney, 1987). Early studies demonstrated adaptations of 5-HT and NE receptors and their secondary messenger systems. However, more recently focus has shifted to downstream targets of these receptors and their second messenger coupled systems (Duman et al., 1996; Duman et al., 1997). Amongst these targets is BDNF which through its powerful influences on neuronal survival and function could play a role in the therapeutic action of antidepressant treatments. Future studies of the role of neurotrophins and other potential downstream targets in depression will lead to the ability to design novel, faster acting therapeutic agents, and contribute to a better understanding of the disorder.

Vaidya Vidita A, Ph.D. Thesis : The Role of Brain-derived Neurotrophic factor in the Action of Stress and Antidepressant Treatment.

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# Ayurvedic Definition and Classification of Manovikara

B. S. Venkataram

Ayurvedic classics are perhaps the oldest repositories of systematic and clinically useful documentation on Manovikara (mental disorders), although one could find some useful information related to these conditions in the Vedas. Caraka<sup>1</sup> (500 B.C.) states that, "treatment for Manasavyadhi should be sought through experts in that field." Chakrapani<sup>2</sup> (11 A.D.), commenting on this statement, uses the term "Manasavyadhi-bheshajavedee." These textual references prove that psychological medicine was an area of specialization and that psychiatrists existed in the past. Unfortunately, due to historical reasons, the ancient Ayurvedic works dealing exclusively with Manas (the mind) and Manovikara (mental disorders) are not available. Therefore, one is constrained to cull out the relevant material scattered in the Ayurvedic classics to throw more light on this area of study.

Roga is defined as "painful experience" or the "imbalanced state of Dosha (mental or physical elements)." This definition is applicable to both Sariravikara (physical illness) and Manovikara (mental disorders). It also implies that both Sarira (body) and Manas (mind) are involved in all physical and mental diseases. Still, considering the predominance of the Dosha involved, diseases are termed as Sariraja (physical), Manasa (mental), and Ubhayatmaka (dual type). Accordingly, Manovikara can be defined as an imbalanced state of Rajas (passion) and Tamas (inertia). Some of the Manovikara, like Unmada (psychosis) and Apasmara (epilepsy), have been well defined and described in the classics, while some of them, like Cittoddvega (anxiety), Krodha (anger), and others have been mentioned just by name without other essential details like Nidana (etiology), Purvarupa (prodromal features), Rupa

(clinical profile), and Cikitsa (treatment). Therefore, it is necessary to formulate a workable definition common to all Manovikara in general and classify them to facilitate accurate diagnosis and effective management. This paper attempts to discuss these two aspects.

Pathak, has given a descriptive account of Manas according to the principles of modern clinical psychology.<sup>3</sup> Definition and classification of Manovikara do not find a place in this work.

Lakshmipati dealt with different aspects of the mind in relation to Yoga.<sup>4</sup> Mental dispositions, classification of emotions, Prakrti (personality), classification of mind disorders in modern psychology, and the three types of Ayurvedic therapies described in Ayurveda. However, Ayurvedic definition and classification of Manovikara are not described.

Achal did not define Manasa Roga (mental illness) but classified it into two types Ekadeshiya Manasika Roga and Ubhayasrita Manasikaroga.<sup>5</sup> The various emotional excesses of Kama (desire), Krodha (anger), and others have been grouped under Ekadeshiya Manasikaroga; Anidra (insomnia or sleeplessness), Bhrama (giddiness), Madatyaya (alcoholism), Unmada (psychosis), Apasmara (epilepsy), and so forth have been grouped under Ubhayasrita Manasikaroga. Advantages of this classification are not explained, but such diseases in the Ayurvedic classics which could be considered as Manovikara have been compiled and presented.

Singh, considers Manasa Roga under Bhuta Vidya (management of seizures and other mental disorders induced by evil spirits or nonhuman influences),<sup>6</sup> quoting other authors in support of his view. There is no definition of Manovikara in his book. Manasa



Roga have been classified as mild abnormalities and severe abnormalities. Dhanyakurnar Ijari, has not defined Manasa Roga but has grouped Manasavikara under two categories-Manoroga and Laghurmanovikriti.<sup>7</sup> These classifications appear to have been made on the outdated psychiatric distinction between major and minor psychiatric disorders.

Gupta, has not provided any definition of Manasa Roga but has classified it into four groups, namely, diseases with primarily mental origin and predominantly mental symptoms, diseases with primarily mental origin and predominantly physical symptoms, diseases with primarily physical origin and predominantly mental symptoms, and diseases with primarily physical origin and predominantly physical symptoms.<sup>8</sup> Conditions assigned to each of the groups have been described in detail.

Singh, defines Manasa Roga as "that condition, wherein abnormalities mainly related to Manas (mind) are reflected."<sup>9</sup> The conditions due to psychological factors but reflected mainly as physical manifestations are termed Manodaihik Roga. The following four types of Manasa Roga have been suggested based on the observations made on mental patients and the description available in the Ayurvedic literature: Manasa Roga caused by primary vitiation of Rajas (passion) and Tamas (inertia); Manasa Roga due to imbalance of Rajas and/or Tamas as well as the Tridoshas-the elements-Vata, Pitta, Kapha; abnormalities related to Manasa Prakriti (psychological constitution); and Manodaihik Roga due to mental disturbance but reflected as physical signs and symptoms. Lists of clinical conditions assigned to each of these classifications with their nearest equivalents in psychiatry are also provided.

### **Definition of Manovikara**

Caraka's description of Unmada as the unsettled condition of Mana (mind), Buddhi (intelligence), Sanjnajnana (orientation and responsiveness), Smriti (memory), Bhakti (desire), Sila (habits and temperament), Cesta (psychomotor activity), and Acara (conduct) serves as a prototype definition for all Manovikara in general, since one or more of

these aspects get affected in all types of Manovikara.<sup>1</sup>

The classical description available when compiled and arranged cohesively leads to the conclusion that, in all Manovikara, participation of Alpasatva (weak psyche), vitiation of Manodosha (mental elements)-Rajas (passion) and Tamas (inertia) - or both Manodosha and Sariradosha, Manovahasrotovaigunya (vitiation of pathways of the mind), and Manahkarmavikriti (impairment of functions of the mind) will be common.

Therefore, Manovikara (mental disorder) according to Ayurveda can be defined as an abnormal mental condition characterized by a) the presence of Alpasatva (weak psyche) as a premorbid factor; b) vitiation of Manovahasrotas (pathways of the mind); c) morbidity of the Manodosha alone or both Sarira and Manodosha; and d) involvement of one or more of the eight aspects considered in the definition of Unmada (psychosis) reflecting the functional impairment of the Manas (mind). The presence of Alpasatva, vitiation of Manovahasrotas, and involvement of Manodosha/Sariradosha are inferred depending on the degree of functional impairment of the Manas reflected through abnormal Sila (habits and temperament), Cesta (psychomotor activity), and Acara (conduct) and others.

### **Classification**

Classification of diseases is an interesting and important area of study. In Ayurveda, diseases are classified on the basis of various aspects like Nidana (etiology), Adhisthana (seat of origin), Sadhyasadyata (prognosis), intensity, involvement of the Doshas, Srotas (channels), and others. Understanding these details will be richly beneficial in diagnosis and management.

According to Sushruta, diseases are classified into three major categories-Adhyatmika (constitutional), Adhibhautika (environmental), and Adhidaivika (providential). Adibala (genetic), Janmabala (congenital), and Doshabala Pravritta (Dosha induced) are the three subtypes of Adhyatmika conditions. The Sanghatabala Pravritta (trauma induced) condition comes under the Adhibhautika type. Swabhava bala Pravritta Daiva bala, and kalabada pravritta Pravritta (physiological) are the three subtypes of



Adhidaivika conditions. In general, all the diseases can be grouped under one of these classifications. Sushruta has also classified diseases into two kinds as Shastrasadhya (surgically treatable) and Snehadisadhya (medically treatable) (S.Su. 24). Under another classification, he describes diseases as four types: Agantu (exogenous), Sarira (physical), Manasa (mental), and Swabhavika (natural) (S. Su.1).

In yet another context, Sushruta considers diseases as two kinds considering their Adhithana (base of genesis) as Sariradhithana (body based) and Manoadhithana (mind based). Commenting on this, Dalhana<sup>10</sup> explains Jwara (fever) and others as Sariradhithana, Kama (passion) and others as Manoadhithana, and Unmada (psychosis) and others as Ubhayadhithana (dual type, mind and body based) (S.Su.1/26 + Dalhana's commentary). The terms Manoadhithita- and Ubhayadhithita- used in this paper as a prefix to Manovikara (mental disorders) are based on this reference.

Caraka, on the other hand, has classified diseases as Nija (endogenous), Agantu (exogenous), and Manasa (psychological) (C. Su.11.)<sup>1</sup> This classification is based on the etiology. Nija (endogenous) Rogas are those which are engendered due to irregular food habits and psychobehavioral excesses resulting in the impairment of the Sarira-dosha (physical elements). Agantu (exogenous) Rogas are those caused by extraneous factors such as injuries, poison, fire, and wind. Manasa (psychological) Rogas are those which occur due to the gain of undesired objects or losing the desired/ cherished ones, resulting in the impairment of the Manodosha (mental elements).

Diseases have also been classified into three types - Sarirashraya (body dependent), Manoashraya (mind dependent), and Dwayashraya (dual type)-depending on their Adhithana (base of genesis). Sarirashraya conditions are Kushtha (dermatitis), Atisara (diarrhea), and others. Manoashraya conditions are Kama (passion), Krodha (anger), and others. Dwayashraya conditions are Unmada (psychosis), Apasmara (epilepsy), and others (C.Su.1/55 + Chakrapani's<sup>2</sup> commentary; C.V.6).

In conclusion, it can be said that diseases

are termed Saririka (physical) or Manasa (psychological) on the basis of Nidana (etiology), Adhithana (seat of origin or genesis), or involvement of respective Doshas (elements), separately or in combination. Ubhayatmaka (dual type) Rogas are those wherein both Sarira (body) and Manas (mind) are affected due to the involvement of both Sarira and Manodoshas (physical and mental elements).

All these classifications ultimately aid better management of diseases. It is not possible to strictly categorize diseases as physical or mental since they affect the living body, which is a combination of body, senses, mind, and self wherein even if one of them is disturbed, the remaining three are also affected.

Classifications of only some of the Manovikara such as Unmada (psychosis), Apasmara (epilepsy), Murcha (fainting), and a few others are well documented in the classics. However, after a critical study of the classics, it is possible to classify Manovikara (mental disorders) into two major categories: Manoadhithita (mind based) Manovikara (MMV) and Ubhayadhithita (dual type) Manovikara (UMV). UMW can be further classified into two subtypes: Manosarir-adhithita (mind, body based) Manovikara (MSMV) and Sarira-manoadhithita (body, mind based) Manovikara (SMMV). Conditions that could be considered under each of the categories are listed below.

- MMV-emotional neurotic disorders  
Krodha (anger), Lobha (greed), Abhyasuya (cynicism), Moha (infatuation), Kama (passion), Shoka (grief), Vishada (lassitude), Bhaya (fear), Mana (pride), Dainya (helplessness), Matsarya (hostility), Mada (arrogance), Harsha (jubilation), Cittodvega (anxiety), Irsha (jealousy), and so forth

(C.V.6, S.Su.1).

- UAW-dual-type conditions
  - a. MSMV-psychosomatic/somatized neurotic conditions  
Jwara (different kinds of fevers) induced by Kama (passion), Krodha (anger), Shoka (grief), Abhishapa (curse), Abhichara



(sorcery), Atisaras (different kinds of diarrhoea) due to Bhaya (fear-induced), Shoka (grief), Shokaja Shosha (grief-induced emaciation), Stanyanasha (loss of lactation), Palitya (premature graying), and others

(C.C.3, C.C.19, S.U.41, V.U.23)

b. SMMV-somatopsychic conditions

Unmada (psychosis), Apasmara (epilepsy), Madatyaya (alcoholism), Bhrama (giddiness), Sanyasa (syncope), Atatvabhinivesa (delusions, paranoia, hallucinations), Murcha (fainting), Aswapna (insomnia), Mada (intoxication), Tandra (stupor), Atipralapa (prating), Jalatrasa (hydrophobia or rabies), Anavasthita Cittatva (fickle mindedness), Vishaja Unmada (toxic psychosis), Nindra-dhikya (hyper-somnia), Ashabdashravana (auditory hallucinations), Apatanaka/ Apatan-traka (puerperal psychosis), and others

(C.Su.20, C.Su.24, C.N.7, C.N.8, C.C.9, C.C.10, C.Si.9, S.K.7, S.U.62)

Some of the Nanatmajavikara (disease states caused by a single imbalanced or vitiated Dosha) considered by Ramu et al. as one of the four types of Manovikara (mental disorders) are included here under SMAW, since their causation and treatment are similar to those of SMW.<sup>11</sup>

## Discussion

In MMW, the exaggerated emotions, like Kama (passion) and Krodha (anger), entertained by the individual with Alpasatva (weak psyche) cause the initial impairment of Manodosha (mental elements). Involvement of Sariradosha (physical elements) will be secondary and minimal. Swanigraha function of Manas (mental control) is affected and reflected as impairment of Sila (habits and temperament) and Cesta (psychomotor activity). Indriyabhighraha (perception and motor functions), Ooha (anticipation), and Vicara (thought process) are not much affected. MMV conditions present as emotional or neurotic disorders. The Prakrti (personality) is well preserved in MMV

patients. They are aware of their problems and motivated to approach the therapist. MMV patients extend cooperation and play an active role in the treatment.

MMV are effectively treated with well-planned Satvavajaya Cikitsa (psycho-behavioral therapy) and Daivavyapashraya Cikitsa (divine therapy) (table 1). Yuktivyapashraya Cikitsa (diet-drug therapy) with palliatives will also be required as a secondary, supplementary therapy.

The best suited Satvavajaya Cikitsa (psycho-behavioral therapy) measures are Santvana (consolation), Asvasana (reassurance), Vismriti (diversion), and Sadvritta (code or virtues) related to the individual's personal and social behavior in terms of Sila (habits and temperament) and Acara (conduct). These measures enhance the mental potentials such as Jnana (knowledge of self, Vijnana (professional knowledge), Smrti (memory), Dhairya (self-confidence), and Samadhi (concentration) of the patient and subdue the causative exaggerated emotions. In other words, these measures enhance the state of Satva (pure consciousness) to weaken the dominance of Rajas (passion) and Tamas (inertia) in these patients.

MSMV are also caused in an individual with Alpasatva (weak psyche). Initially the Manodosha (mental elements) get highly disturbed due to sudden and intense emotional factors. Swanigraha function of Manas (mental control) is affected and reflected as impaired Sila (habits and temperament). The disturbance is reflected as physical disorder with moderate degree of involvement of Sariradosha (physical elements). Like those with MMV, these patients will be aware of their problems, approach the therapist, and remain cooperative during the period of treatment. MSMV conditions require initial diet-drug therapy with emphasis on palliatives instead of purificatory measures. MSW are not relieved until the primary impairment of Manodosha (mental elements) is resolved: psycho-behavioral therapy plays an important role. Satvavajaya Cikitsa measures used in the treatment of MMV are beneficial in MSMV conditions as well. Daivavyapashraya Cikitsa also may be helpful in these conditions.



**TABLE 1.** -Comparative description of Manovikara (mental disorders).

MMV (Emotional-neurotic disorders)	MSMV (Somatized neurotic conditions)	SMMV (Psychotic conditions)
Causes: a) Mithya Vihara (behavioral excesses) and b) Alpasatva (weak psyche)	As in MMV	a) Mithyahara (unwholesome food) and Mithya vihara (behavioral excesses). b) As in MMV
Primary imbalance of Mano dosha (mental elements) secondary minimal imbalance of Sariradosha (physical elements).	Sudden intense imbalance of Manodosha with moderate imbalance of Sariradosha.	Gradual imbalance of Sariradosha and Manodosha.
Manovahasrotovaigunya (vitiating of the pathways of the mind).	As in MMV.	As in MMV.
Swanigraha (mental control), Vicara (thought process) affected; reflected as impaired Sila (habits and temperament) and Cesta (psychomotor activity).	Swanigraha affected; reflected mainly as impaired Sila.	All functions of Manas (mind) affected; reflected as impairment of Sila, Cesta, and Acara (conduct).
Manifested as emotional disturbance	Manifested as physical condition.	Manifested as mental derangement with certain distinctive physical features.
Prakriti (constitution), insight, motivation-all intact.	As in MMV	Personality affected, motivation absent and insight poor.
Well managed with primary collaborative psychobehavioral therapy and secondary concurrent palliative diet-drug therapy.	Well managed with primary palliative diet drug therapy and concurrent collaborative psychobehavioral therapy and divine therapy.	Managed with primary diet-drug therapy with active purificatory and divine therapy. Prescriptive psychobehavioral therapy required as short and long measures

SMMV are caused mainly due to the gradual vitiating of Sariradosha (physical elements) as a result of unwholesome food habits cultivated ignoring the "eight point directives related to food" suggested by Caraka.<sup>1</sup> The vitiated Dosha (elements) along with Alpasatva (weak psyche) already present in the individual occlude Manovahasrotas (pathways of the mind) and cause imbalance of Manodosha (mental elements). As a result, the functions of Manas (mind) are impaired

and reflected as the unsettled condition of one or more of the eight aspects of Manas in the definition of Unmada (psychosis). In SMMV patients, Prakriti (constitution) is affected unlike in other types. These patients are not adequately aware of their condition (lack of insight) and are brought to the therapist by others (amotivation). SMMV patients are generally indifferent to treatment, often noncooperative, and play only a passive



role in the management. SMW conditions are relieved only when the occlusion of Manovahasrotas (pathways of the mind) is removed by diet-drug therapy with primary purificatory and secondary palliative components on the other hand, may also play a significant role in the more frequently encountered conditions like Unmada (psychosis) and Apasmara (epilepsy) as they are considered to have originated due to divine wrath, according to Caraka.<sup>1</sup>

Psychobehavioral therapy measures such as Vaismaya (showing wonders), Adbhutadarshana (showing marvels), Bhaya (scaring), Bruyadistavinasham (announcing the loss of someone/something dear to the patient), Vismrti (distraction), Tarjana (verbal threatening), Trasana (frightening), Tadana (whipping), and Kupavasa (solitary confinement) will also be immensely helpful depending on the mental status of the patient. Satvavajaya Cikitsa measures are intended to rapidly induce mental stimulation or diversion. Since these measures cause intense stimulation, they are generally not tolerated well by the patients. They help the excited or withdrawn patients to become docile and responsive to treatment, rather than in enhancing Satva (pure conscious) directly.

Thus, as seen above, the various psychotherapeutic measures recommended in Ayurveda can be classified as collaborative—those beneficial to patients who are aware of their problems, and prescriptive—those beneficial to patients who are not aware of their conditions.

Treating the various emotion-induced conditions by evoking opposite emotions as suggested by Caraka (C.Ci.9) should be thoughtfully designed, as all the emotions are generally interlinked and are themselves termed "Roga" (V.Su.1).<sup>1</sup> However, this approach may be useful in inducing quick diversions in some of the patients.

It is necessary to remember that all diseases, either physical or mental, are caused by one or more of the three etiological factors: Asatmyendriyarthasamyoga (incompatible physical, verbal, and mental activities), Prajnaparadha (deliberate erring), and Parinama (seasonal variations). Similarly, all three treatments—divine therapy, diet-drug therapy, and psychobehavioral therapy—can be employed in all diseases either physical or mental. The treatments are to be chosen judiciously depending on the type of illness.

## Summary

The definition and classification of Manovikara (mental disorders) are presented in this paper based on the classical descriptions available. The basis of classifications and their usefulness for better understanding and effective management of different Manovikara is highlighted. This work is expected to be of immense guidance to the practitioners, teachers, and researchers working in the areas of mental disorders.

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"Management of mental disorders involves essentially the same steps outlined for physical treatment. When poor mental digestion has created many untoward emotions and the accumulation of those emotions eventually distorts self-image and the ability to function efficiently; removal of the cause is the first requisite... There is even a mental Triphala to help scrape away the old Ama of selfish attachments. It is called Kirtana, the devotional signing of God's name.

- Robert Svoboda



# **Etiology, Classification, Definition of Mental Disorders (Ayurvedic Concept)**

**C. P. Shukla**

In Ayurveda and other Vedant literature, Manas (the mind), Mana-Artha (objects, functions of the mind), Karma (actions of past lives), functions of mind, the mode of working, Niyabhigraha (mind control over sensory and nigraha (motor organs), the method of Manonigraha itself, and Manovikaras (mental disorders) and their Cikitsa (treatment) have been elaborately described. It is for the scientists, physicians, and Ovikaras (research scholars) to understand, to treat the patients, and to conduct research on the above and work for the benefit of mankind.

## **Manas (Mind) and Its Functions**

Any living being on the earth is composed of three main components: Satva (mind), Atma (spirit or soul), and Sarira (body). These are like a tripod on which all living creatures stand. The Samyoga (combination or unification) of these three in the human being is called Puman or Cetana. This principle is the Adhikarana (main foundation) of Ayurveda.

The Indriyas (sensory and motor faculties) are necessary for proper functioning of a human being. Their structural and functional integrity (Samyoga) is called Dhail and Jivita (life). Life is a continuous process (Nityaga) and continuum (Anubandha). Thus, Satva (mind) has been given great importance in all living beings and especially in human beings. Even animals such as the cow, ox, and buffalo have minds, but the development of the mind in human beings is maximal. A human being can express feelings such as likes, dislikes, thoughts, and desires, but an animal cannot.

## **Mano-Arthas (Objects or Functions) and Gunas (Qualities) of the Mind**

The functions of the mind are very diverse and complex. The mind works with the sense objects to gain knowledge. Ideas change very

often. The elements Satva (purity), Rajas (passion), and Tamas (inertia) change often in the same person. That is why it may be felt that there is Aneka (more than one mind in the body). But this is wrong. In the same way, the mind seems to work at many places and also think in various ways. This creates doubt that Manas is Vibhu (all pervasive). But both of these qualities are false. The mind cannot work at the same time on many things, cannot concentrate on many things at the same time. So the mind is Anu (one) and Eka (a single entity).

Artha (objects, functions) of the mind are Chintya (thinking), Vicharya (thoughtfulness), Oohya (discussion), Dheyaya (insight), Sankalpya (conclusion-drawing), and any other things to be known by mind.

Indriyarthas are the functions of the sense organs. The five sense organs are the eyes, ears, nose, tongue, and skin. The functions of the organs are seeing or observing, hearing, smell, taste, and touch, respectively. The inputs (objects) reach the mind, the mind analyses the object, and knowledge is gained.

Sankalpa (decisions) are made according to Kala (time) and Desha (place). The decisions are various and diverse.

Satva-Rajas-Tamas are the temperaments or Manas Doshas (mental elements). The mental elements or temperaments may be changed at the same time or at different times or according to Desha (place), atmosphere, circumstances, and Kala (time). A person is classified as Satvik, Rajasika, or Tamasika according to the predominance of the type of Manas Dosha. For example, the Satva quality is Laghu (light) so that the person may be light in nature, ready to gain knowledge, and sees objects in a correct manner. The Rajas quality is of unstable nature, and the Tamas quality is mainly Guru (heavy) and obscuring.

The functions of mind are Indriyabhi-



ghraha (perception and control of the sensory organs), Swanigraha (control over the mind itself), Ooha (discussion of pros and cons), and Vicara (thinking deeply). Afterward, the Buddhi (intellect) acts and decision is made.

The changes in temperament and mood affect the body, and these changes may produce diseases such as the psychosomatic disorders. In the same way, the body or physical disorders disturb the mind and produce disorders.

### **Etiological Factors of Manasa Rogas (Mental Disorders)**

The Shad-Ripu (six mental conditions) are considered to be the main causes of mental disturbances. They are Kama (desires), Krodha (anger or irritability), Lobha (greed), Moha (infatuations, likes, and dislikes), Mada (ego or arrogance), and Matsava (jealousy). Of the six, excessive desire or nonfulfillment of desire is the greatest and most important factor in causing Manasa Rogas (mental disorders).

Kama (desire) or Upadha (different types of desires) are the greatest cause of Manasa Rogas, says Charaka in Sarira Sthana (chapter 6). Upadha is the main etiological factor that produces mental pain in an individual. Tyaga (renunciation) of all types of Upadha (desires) removes all types of physical and mental disturbances.

Upadha hi paro hetuh Dukhadukhashraya-  
pradhanal !

Tragah sarvopadhanam chu sarva Dukha  
vyapohakah

(Ch. Sha.1).

Charaka compares Upadha (desires) with a cobweb. He says, "Koshakaro yathahyam shunupadhe Vadhaprada Upadahe yatharthebhyastrshuamajnah Sadaturah" (Ch.Sha.1). Thus, the main cause of the majority of mental and psychological diseases is nonfulfillment of one's own desires.

Here one point requires clarification. Some people believe that supernatural elements such as demons, gods, and ghosts enter the body and produce mental disorders. Although Charaka describes mental disorders

disturbances caused by the entering of god) and Bhuta Unmada (due to ghost, etc.), he clearly states that "neither the gods, Grahas (planets or deities), Pishachas (goblins), demons, nor other such elements torment the individual, who is not already tormented" (Ch.Nid. 7). This Shloka (verse) clearly states that the belief that nonphysical elements can enter the body is wrong. It is the psychology of the person that behaves in a particular way. The unenlightened person believes that a particular element has entered the body. In fact, the symptoms or behavioral abnormalities resemble those in the supernatural elements, but these elements can never enter the person.

### **The Doshas (Mental Elements)**

The biochemical substances produced during nerve functions and in the brain may provoke the Doshas which may disturb mental function also. According to Sushruta and Vagbhatta, Sadhaka Pitta is responsible for mental and nerve functions. Vagbhatta says, "Buddhi Medha Abhimanadyai Abhipretartha Sadhanam Sadhakam Hridgatam Pittam."

Sadhaka Pitta is responsible for Buddhi (intelligence), Medha (remembrance), Abhimana (ego-superego and performance of function for achieving the goal). Bhela has described Alochaka Pitta and divided it into two parts: Chakshur Vaisheshika (physical observation) and Buddhir Vaisheshika (internal perception). The Individual can see the substances which are not visible. The development of the mind is so great that he can see from a very great distance or even into the future. This is called the sixth sense or extrasensory perception. Some people have an intuition by which they can forecast events. Thus, Buddhir Vaisheshika and Chakshur Alochaka Pitta are concerned with decisions, other mental functions, and supernatural functions. The nature of the biochemical substances which are produced during mental functions is a matter for further research.

### **The Etiological Factors of Manovikaras**

Acharyas (teachers) of Ayurveda have



summed up the etiology of Manovikaras (mental disorders) into three types: Asatmyendriyarthā Samyoga (unwholesome contact [abnormal, excessive, or faulty use] of sense organs with objects); Prajnaparadha (volitional misuse of body, mind, and speech); and Parinama (abnormal changes in body as a result of time factors such as chronobiology, diurnal rhythms, and seasonal variations).

### **Classification of Manovikaras**

The mental disorders can be divided into three classes: Adhyatmika (constitutional), Adhibhautika (environmental), and Adhidaivika (providential). Adhyatmika disorders are classified according to an individual's constitution; Adibala Pravritta (genetic), Janmabala Pravritta (congenital), or Dosha-bala Pravritta (functional, due to vitiation of the Doshas). Adhibhautika disorders are classified according to environmental or external factors such as trauma and insect bites). Adhidaivika disorders are classified according to Swabhabala Pravritta (natural or inherent factors such as age, for example, senile degeneration causing senile dementia), Kalabala Pravritta (seasonal factors), or Daivabala Pravritta (providential or idiopathic factors).

### **Definition and Classification of Manovikaras**

The disorders related to the behavior of an individual are considered to be mental disorders. Failure to make satisfactory adaptations to life, the environment, or to other members of society are considered to be mental or psychological disorders.

According to Ayurveda, the Manovikaras (mental disorders) can be classified into four main groups: Unmada (psychoses) -diseases associated with excitement, depression, or predominance of ideas; Atatvabhinivesa (obsessions)-mental disorders associated with wrong judgement due to anxiety, neurosis,

neurasthenia, obsession, and abnormal behavior; Apasmara (convulsive disorders) -diseases interfering with memory, knowledge and so forth, with the main symptoms being convulsions and either transient or long-term loss of memory or retention power, or mental retardation; Mada-Murcha-Sanyasa (comas)-giddiness or vertigo, unconsciousness, and coma. These disorders may be purely psychic or psychosomatic, associated with other types of physical disorders. This requires further research. The treatment of all of the types of mental disorders have been given in detail, but this requires a separate and long discussion.

In conclusion, it may be said that a thorough study of all literature in Ayurveda and ancient literature such as Bhagwad-geeta and Upanishada is required in order to understand the physiology of the mind and the pathological changes. As said previously, psychology and temperament have a great impact on the body and its functions. For example, hypertension; certain types of heart diseases; digestive disorders such as hyperacidity, indigestion, peptic ulcer, Shokaja atisara (ulcerative colitis), Bhayaja atisara (irritable bowel syndrome), and many other digestive disorders; liver diseases such as gall stones; sexual disorders; and certain types of skin diseases are either caused or provoked by an impaired mental state and are called psychosomatic disorders. That is why Caraka says "Sarira (body) affects psyche and psychology affects the body."

The treatment of most psychological and psychosomatic disorders is to pacify the mind. The best way for tranquilizing the mind is Dhyānāyoga (meditation), an important procedure of Yoga. There are three methods of pacifying the mind: Dhyānāyoga (meditation), Hāthāyoga or Ekagrata (concentration), and Stuti (contemplation or prayer). Of these three, Dhyānāyoga is the safest way for pacifying the mind. There are medicinal treatments also, but the subject is lengthy and is not discussed here.



# Implications of Ayurvedic Classification of Schizophrenia

H. Mukundan and S. M. Channabasavanna

Caraka, in his Ayurvedic treatise, Caraka Samhita, defines insanity as excessive wandering of intellect, mind, and memory (C.Chi.8).<sup>1</sup> Mental disorder is caused by the disintegration between body, mind, and senses, which ultimately disturbs the self. Consequently, there are disturbances in the mind, awareness, perception, knowledge, memory, conduct, and behavior of the individual. It is also suggested that disturbances in these functions may be present in different degrees.

Caraka further describes Unmada (Ch. Ni.7-4) as the disturbed or the impaired condition of the Manas (the perceptual cognitive faculty), Buddhi (the intellectual judgmental faculty), Sanjnanana (orientation), Smriti (memory), Bhakti (insight), Sila (habit), Cesta (psychomotor activity), and Acara (conduct). The former six are the mental functions, whereas the latter three are the behavioral expressions of the disturbed mental state.

Caraka has suggested two levels of classification of the different aspects of diseases: intensity (severe or mild), location of the affliction (mental or bodily), etiology (endogenous or exogenous), and seat of origin (gastrogenic or endogenous). Caraka and Sushruta<sup>2</sup> (Sush. Sam.) have both summarized the endogenous etiologies as Sahaja (acquired at conception) or Nija (acquired at a later stage), which are caused by the discordance of the Tridosha (the three pathogenic elements). The severe form of mental illness, also known as Doshajonmada is caused by the imbalance of the three Doshas. There is a remarkable emphasis on the various biological and physiological factors that one has inherited and the lifestyle of the individual in the genesis of mental illness.

This study was undertaken for the purpose of subtyping schizophrenia on the basis of Ayurvedic concepts of classifications of Unmada (serious type of mental illness or psychosis). An attempt was made to classify schizophrenic patients using an Ayurvedic symptom list, to determine the association of this classification with the positive and negative syndrome scale scores (PANSS<sup>3</sup>), and to compare the neuropsychological deficits in the subtypes. It was postulated that PANSS and the neuropsychological test profiles would support the validity of the Ayurvedic classification of schizophrenia.

## Material and Methods

The sample consisted of 85 patients who satisfied the criteria for schizophrenia according to the International Classification of Disease-9 (ICD-9).<sup>4</sup> The subjects consisted of 48 males and 37 females. Ages ranged from 18 to 45 years, with a duration of illness ranging from 2 months to 2 years. All patients were literate. Patients were excluded from the study on the basis of a past or present diagnosis of mental illness other than schizophrenia, or neurological disorder, a history of head injury or trauma, or regular psychoactive substance or alcohol abuse. As per ICD-9, they were subtyped as Hebephrenic (n=15), Catatonic (n=13), Paranoid (n=37), and Unspecified (n=20).

The first step in Ayurvedic diagnosis is the evaluation of the premorbid personality of the affected person. For this purpose, a personality questionnaire called Kapha, Pitta, Vata Prakrti in Ayurveda,<sup>5</sup> was administered to each patient. This questionnaire helps to identify four types of personality—the Vata, Pitta, Kapha, and the mixed type. The details of the questionnaire are given below. Out of 85 schizophrenics, 60 had predominantly



Kapha, Pitta, or Vata personality, and these patients constituted the final sample for the study.

For comparison of neuropsychological test performance, a control group of 30 normal subjects matched for age and education was determined. The clinical interview of the patient and the interview of the collaterals comprised the following tools:

- A standardized form was used for the collection of the sociodemographic variables and other illness-related history.
- The PANSS.
- The Unmada Samanya Lakshana checklist and a modified version of Unmada Roga Vinishchaya Rugnapatrika.

#### **Kapha Pitta Vata Prakriti Questionnaire**

This inventory measures the relative position of an individual on Kapha, Pitta, or Vata Prakriti (the type of personality) as described in the Ayurvedic texts. Statements in the inventory are classified into three lists. Each list consists of 30 statements, making a total of 90 statements delineating physical appearance, biological functions like sleep pattern and autonomic functions, food preferences, and temperamental, motivational, and volitional attributes of a person which are indicative determinants of personality.

Each statement has to be either answered affirmatively or negatively by the patient, or the interviewer has to arrive at a score based on the observation of the attribute in the patient or the interview with the collateral. For example, certain statements like the color of the eyes or hair, the texture of skin or hair, were noted by the interviewer.

Statements such as "the patient grinds teeth," "is restless in sleep," "completes a task on hand," or "is generally enthusiastic" were answered by the informants, whereas statements like "I like cold things," "I have burning sensations in my hands and feet," or "I like to eat fried food" were answered by the patient. A person with a positive score above

73 percent in any one category and below 27 percent in the other two categories is considered to have predominantly the first type of personality.

#### **Unmada Samanya Lakshana Samucchaya**

The general symptoms of Unmada (psychosis), which are examined to broadly identify the patient and to arrive at a diagnosis of Unmada, are called Unmada Samanya Lakshana, as mentioned in the Ayurvedic texts (C.Ci.6.7). The symptoms of Unmada include impairment in the functions of Manas (perceptual cognitive faculty), Dhi or Buddhi (the intellectual judgmental faculty),<sup>6</sup> Dhrti (retention of information), and Smrti (memory), and the resultant behaviors. The behaviors were implied in broadly categorized symptoms such as impaired perception and cognitive functions, volitional instability, blank look, mental blankness, fear, thought disorder, indifference, and purposeless activity. A person who had these impairments and behaviors was considered to have Unmada.

#### **Unmada Roga Vinishchaya Rugnapatrika**

This symptom list is the modified version of the Unmada Roga Vinishchaye Rugnapatrika.<sup>7</sup> It constitutes the list of symptoms of Unmada (psychosis) which deal with the three Doshaja Unmada-Vatajonmada, Pittajonmada, and Kaphajonmada-according to Ayurvedic methodology compiled from the ancient Ayurvedic texts, viz., *Caraka Samhita*, *Sushruta Samhita*, *Astanga Hridaya*, *Astanga Sangraha*, *Madhava Nidana*, *Bhela Samhita*, *Yoga Ratnakara*, *Rasaratna Samucchaya*, and *Hamsaraja Nidana*. This symptom list was further modified<sup>8</sup> for the purpose of this study after consultation with the Ayurvedic Vaidya (physician) (B.D.Nanal, personal communication; C.G. Joshi, personal communication). The assessment procedure involved observation of physical manifestations, interpersonal behavior, cognitive and verbal output, thought content, and response to structured questioning in addition to information collec-



ted from the collaterals. It also involved direct observation of Sila (habits, personal care, affective behavior, biological functions, and physiological functions), Cesta (psychomotor activity which includes general motor activity, facial expression, posture, and speech), Acara (conduct as defined by social standards and controlled by volition), and lastly Manas, the main attributes of which are Buddhi (intellectual judgmental functions), Smrti (memory), Indriyabhighraha (perceptual motor functions), Swanigraha or Manonigraha (mental control), Ooha (anticipation), Vicara (thought process), Indriyani-rapeksha Ayatarthajnana (delusion), Sanj-najnana (orientation and responsiveness), and Bhakti (insight).

### **Neuropsychological Assessment**

The neuropsychological battery<sup>8</sup> consisted of tests for assessing deficits in the areas of attentional processes, process control, visual spatial functions, visual integration, learning and memory functions, concept formation, and thought processes. Some of the tests were Auditory vigilance, Trailmaking, Digit span, Number scanning, Visual search, Series completion test, Ideational fluency, Visual and verbal learning and memory functions, Block design, Drew's, and Visual exploration.

## **Results**

The Unmada symptom checklist indicated that out of 23 Vata Prakriti patients, 18 had predominantly Vatajonmada Lakshana Vata type Unmada (psychotic symptoms). Out of 32 Pitta Prakriti patients, 27 had predominantly Pittajonmada symptoms, and out of 19 Kapha Prakriti patients, 15 had predominantly Kaphajonmada symptoms.

### **Vatajonmada**

The frequency analysis of Vatajonmada symptoms showed that the most frequently seen symptoms were Vak Vikarah (irrelevant, incoherent, excessive speech), Ajasram (wandering tendency), Abhikshanam (out of place behavior like smiling, laughing, and singing), and Sheeghra Sambraham (eager to

start but neither sustain nor complete an activity). These symptoms reflect absence of purpose, irrelevance, excessive talk, and impulsivity in the patients. The total scores of Vatajonmada show a positive correlation with the general pathology scores on PANSS.

Mannerisms and posturing, unusual thought content, disturbances of volition, and poor impulse control are some of the items from the general pathology scale of PANS that are similar to the symptoms described in Vatajonmada. Of the 60 schizophrenics, 50 had at least one and 35 had two of the above symptoms. Eighteen had a preponderance of Vatajonmada, and almost all of them were nonparanoid schizophrenics on ICD-9. The Vatajonmada group significantly differed from the Pittajonmada group on the PANS. The Vatajonmada and Kaphajonmada groups had comparable scores on these scales.

The neuropsychological profile showed that Vatajonmada and Kaphajonmada patients had severe difficulty in undertaking the tests. Vatajonmada patients had difficulty in understanding the test instructions. If they understood the instructions, they had difficulty in approaching the tests in a purposeful and goal-directed manner; they gave up without making any efforts. Their lack of effort was further worsened by inappropriate behavior, irrelevant speech, and poor impulse control.

### **Pittajonmada**

Symptom frequency analysis showed the most frequently presented symptoms were Santarjanam (threatening), Asthan Amarsh/Krodha (inappropriate anger, violence, or excitement), and Akasmat Swesham Paresham Abhihananam (assaultive tendencies).

All the patients were classified as paranoid on the ICD-9. The Pittajonmada profile closely resembles the paranoid symptomatology. It significantly identified the paranoid schizophrenics and hence may be considered to have high specificity with respect to diagnosis of paranoid schizophrenia. Further, within the Pittajonmada group, the scores were found to have a significant correlation with the positive syndrome scale on PANSS. The symptoms of excitement and hostility are the



ones mainly reflected on the Pittajonmada checklist.

The mean negative syndrome score of the Pittajonmada group on PANSS was significantly smaller than that of the Vatajonmada and Kaphajonmada groups, whereas their mean positive syndrome score was significantly higher than that of the other two groups. This clearly demonstrates that the symptoms elicited under the Pittajonmada category are active symptoms of psychosis and hence the significant positive correlation with the positive syndrome score. The neuropsychological profile shows that these patients did well on the neuropsychological tests. Performance of the Pittajonmada subjects was nearly equal to that of the normal control group as seen on several tests. These patients were relatively better preserved at a cognitive level because they interact with others and their environment in general in a more purposeful, meaningful, and efficient way. According to Ayurveda, the Pitta personality is categorized by superior intellect in the form of quick grasping and good memory.

### **Kaphajonmada**

The most common symptoms were Sthanamekadeshe (confinement to one place or posture), Rahaskamata (fond of solitude, remaining secluded, secretive about desires and activities), Shouchadwesa (hatred toward cleanliness, lack of hygiene, poor personnel care), Bibhatswam (loathsome, repulsive, disgusting appearance), Mandagni (complains of tastelessness, rejection of food, loss of appetite, reduced food intake), and Manda Vihar (slow body movement).

The above features clearly show that the description is that of a withdrawn patient, and the negative features of schizophrenia are extremely well captured in this checklist. These symptoms merge well with several symptoms on the negative syndrome scale such as blunted affect, emotional withdrawal, passive, and apathetic social withdrawal. A significant correlation emerged between the scores of Kaphajonmada and the Negative Syndrome scale.

Kaphajonmada patients also had severe difficulty in undertaking tests, but unlike the

Vatajonmada type, they were found to make an effort under repeated commands and instructions. However, their total performance on the tests was significantly deficient and inferior to that of Pittajonmada patients.

The main outcome of the study is the verification of the tenacity of the Ayurvedic method of classification of Unmada. The Tridosha theory appears to classify a disease on the basis of its clinical status. The typology of Unmada offered by this theoretical model strongly correlates with the negative and the positive syndrome status of schizophrenia as shown by the PANSS. The Pittajonmada and the Kaphajonmada patients are found to be associated with positive and negative syndromes, respectively. The Vatajonmada scores have shown a significant correlation with the general pathology score on PANSS.

Vatajonmada emerged as a third dimension of schizophrenia, according to the Unmada typology. The Vatajonmada state is significantly different from that of the Pittajonmada and the Kaphajonmada. The Pittajonmada patient is in a state of inappropriate evaluation of others, showing hostile, abusive, and assaultive reactions, whereas the Kaphajonmada patient is emotionally and physically withdrawn from others, preferring solitude and privacy. The Vatajonmada patient is reactive to the world and others around him, but this is confounded by irrelevant and incongruous behavior and thinking and lack of purposeful behavior. The Vatajonmada patient appears to have symptoms of hebephrenia. The Vatajonmada condition appears to be one for which there may be no straight parallel typology in psychiatric classification. It appears that the major feature of Vatajonmada, in terms of positive and negative states of schizophrenia, is that it has neither positive nor negative features, but has a high score on the general pathology scale.

In summary, Ayurvedic phenomenology effectively identified the symptom profiles in schizophrenia and classified the illness in a way that is acceptable to psychiatric classification. The study confirmed the clinical utility of the classification of schizophrenia using Ayurvedic concepts of the above three types of Doshaja Unmada-ich



Vatajonmada, Pittajonmada, and Kaphajon-mada. The Ayurvedic system has described the effects of vitiation of Tridoshas and systematically categorized these into subtypes giving sharpness to its own diagnostic system. The dimensional approach used in Ayurveda, which was found to be capable of classifying schizophrenia in this study, is considered to be useful in classifying the entire spectrum of mental illnesses. The good agreement seen between the Ayurvedic classification and the positive and negative syndromes in PANSS is a reflection of the strength of the Ayurvedic classification system. As we further examine the Ayurvedic concepts, we find that the concept of dimensionality rather than mutually exclusive subtyping is favored for classifying mental disorders.

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"Don't believe solely because the written testimony of some ancient wise man is shown to you... and don't believe anything on the mere authority of your teachers and priests. What you should accept as true and as the guide in your life is whatever agrees with your Reason mid your own experience, after thorough investigations, and whatever is helpful both for your own well-being and that of other living beings."

- Gautam Buddha



# Reporter Summary 1

## Cultural Translation

The morning session introduced essential concepts and terms used in Ayurveda. Dr. Venkataram presented an overview of Ayurvedic terms and discussed the Ayurvedic concepts of health and illness from the Indian perspective. Drs. Weiss and Shweder discussed the cultural translation of Ayurveda from the Western perspective.

Dr. Venkataram defined the term Ayurveda as the "wisdom of life." Ayurveda encompasses the concept of Swastha, a healthy person, with health defined as a harmony of the mind, senses, and self. The theoretical frame-work of clinical diagnosis in Ayurveda is based on a balance of the Doshas or elemental substances of the mind and body. The mental constitution of a person is based on a balance of the Doshas of the mind-Satva (clarity), Rajas (passion), and Tamas (lethargy). The physiological constitution of a person is based on a balance of the Doshas of the body-Vata (wind), Pitta (bile), and Kapha (phlegm).

Mental illnesses are classified according to the predominant features of the imbalance in Doshas of the Manas (mind) and Sarira (body). The mental disorders are classified as two types: emotional/neurotic disorders in which the primary symptoms involve changes in mental function, such as Unmada-severe mental disorder; and the somatic emotional disorders in which the primary symptoms involve changes in physiology, behavior, and mental function. The classification of mental disorders dictates the treatment and management of the illness.

Dr. Weiss presented Ayurveda as a cultural system that influences the way people think and behave. He discussed clinical diagnosis of mental illness as a framework upon which to make cross-cultural comparisons between Ayurvedic and allopathic medicine. Dr. Weiss described the influences of culture and life

experience on the psychopathology and physical expression of disease and on the clinical approaches to diagnosis and treatment of the illness. The individual's "illness experience" and the doctor-patient relationship figure prominently in the art of clinical diagnosis in Ayurveda.

Dr. Shweder gave an overview of traditions of medicine in India and the United States and discussed the difficulties and hazards associated with cross-cultural translation of multifaceted concepts such as health and disease. He illustrated how the illusion of a shared understanding of cross-cultural terms can lead to an adverse outcome in his example of the "shy girl." He discussed the "big three" explanations of suffering or illness in terms of the biomedical, interpersonal (spiritual), and moral traditions in Ayurvedic and allopathic medicine. He emphasized that the correct cultural interpretation of clinical symptoms and the determination of the correct treatment for the illness must take into account the knowledge base and the belief systems of the individual. Dr. Shweder emphasized that a clear understanding of Ayurvedic terms and concepts will be essential in promoting a productive and meaningful dialog between Indian and U.S. practitioners and biomedical, social, and behavior scientists.

## Discussion

The morning session emphasized the theme of historical transmission of Ayurveda. Ayurvedic medicine was initially passed by word of mouth before it was translated into Ayurvedic texts. Ayurvedic medicine has continued to evolve over its long 2000-year history of practice. Refinements in medical practice over this period give the Ayurveda its great value. In the discussion of the morning session, Dr. Ramachandra Rao referred to Ayurveda as a "medicine for all seasons," a



part of living. He emphasized the need to focus on the fundamental concepts of Ayurveda and the need to fully understand the concepts of Swastha (health) in the purview of Ayurveda harmony between humans and the environment. The concept of "universal morality" or "universal good conduct" was discussed as a necessary link between health and behavior. Dr. Rao stressed the need to "crystallize out" the cultural and biomedical components of Ayurvedic diagnosis and treatment of mental illness-the "what, when, and how to do" of Ayurveda.

The discussion then focused on ways to integrate Ayurveda into the clinical practice of allopathic medicine and vice versa. Dr. Rao discussed the necessity of building two-way bridges. He identified three areas where transcultural approaches could be used to build bridges between India and the United States: clinical diagnoses of mental illness, promoting mental health by diet and good conduct, and pharmacological treatments.

Dr. Rao emphasized the need to integrate Ayurvedic concepts of health and illness with biological constructs of allopathic medicine. He stressed the necessity for an integrative approach drawing upon advances in molecular biology and neuroscience. He suggested that the holistic Ayurvedic approach to illness could provide the framework into which new information (e.g., advances in medical science) could be incorporated.

### **Definition, Classification, and Etiology of Mental Disorders**

The afternoon session focused on the definition, classification, and etiology of mental disorders, comparing the organizing principles of Western and Indian systems of psychiatric diagnosis. Dr. Whybrow presented an overview of the Western, biological psychiatric perspective of mental illness, and Drs. Venkataram and Shukla presented overviews of the Ayurvedic perspective of mental illness.

Dr. Whybrow discussed clinical diagnosis of mental illness from a biological psychiatry perspective using major depression as a model. The clinical features of major depre-

ssion are primary changes in emotion which persist over time and are accompanied by a constellation of secondary behavioral signs and symptoms which also persist over time. The clinical diagnosis is assisted by defining a behavioral and psychological phenotype of the individual based on natural history of the illness, causative factors, and family history. The clinical observations are supported by laboratory tests. Diagnosis of the behavioral and psychological phenotype allows specific treatment and study of the underlying biological processes.

Dr. Whybrow discussed the therapeutic treatment of depression as a combination of factors that assist, modify, or perturb behavioral adaptation to the illness. Therapeutic treatments for depression include factors which assist in behavioral adaptation such as daily routine, regular exercise, psychotherapy, endocrine supplements, hospitalization, and family networks; factors which modify behavioral adaptation and reduce vulnerability to depression such as lithium, some antidepressant agents, light therapy for seasonal affective disorder, and psychotherapy; and factors which perturb behavioral adaptation such as electroconvulsive shock therapy, antidepressant drugs, and sleep deprivation.

Dr. Venkataram classified Manovikara (mental illnesses) according to the imbalance and vitiation of the Doshas. The classification is based upon the Doshas which predominate, Manodoshas (Doshas of the mind) or Sariradoshas (Doshas of the body). He described two classes of mental illness: Manoadhishthita Manovikara (MMV)-the emotional neurotic disorders which are characterized by a primary imbalance in the Manodoshas such as behavioral excesses (e.g., anger, greed, passion, helplessness) and weak psyche (Alpasatva); and Ubhayadhishthita Manovikara (UMV)-the combination or dual type of psychological disorders which are characterized by changes in both the Manodoshas and the Sariradoshas. The sub-variants of the dual type of Manovikara are Manosariradhishthita Manovikara (MSMV)-somatic neurotic conditions-which are characterized by a primary imbalance of the Manodoshas accompanied by a moderate imbalance of the Sariradoshas (physical



symptoms); and Sarira manoadhishthita Manovikara (SMMV) -psychotic conditions- which result from an imbalance of the Manodoshas and Sariradoshas and are accompanied by mental derangement- Unmada, hallucinations, and hypersomnia. These classifications of mental illness permit the employment of different treatment strategies and better management of the illness. The treatment strategies consist of purification and palliative, preventative, and curative interventions, including diet, drugs, and psychobehavioral therapy.

Dr. Shukla presented a different Ayurvedic classification of mental illness based on behavioral signs and symptoms of the disease rather than on an imbalance and vitiation of the Doshas. Within this classification system, there are four main groups of mental and psychological illnesses, including Unmada as one of the groups. The underlying etiological factors which contribute to expression of the mental disorders include factors which influence the mind and its function, such as inability to fulfill a strong desire (all types); genetic or congenital factors; external forces such as stress and unknown environmental factors; and providential factors.

### Discussion

In the afternoon discussion, Dr. Patwardhan emphasized the need to focus on the clinical aspects of Ayurvedic medicine rather than on the historical perspectives in order to develop new clinical insights into the treatment of mental illnesses. He suggested that the focus should be on clinical diagnoses-objective evaluations of the behavior and signs of mental illness, taking into account the

"illness experience" of the patient; and clinical practices the "how, when, and what" of pharmacologic treatment of mental illness in Ayurveda. Dr. Patwardhan stressed the need to develop a new, standardized vocabulary or lexicon to describe the clinical diagnosis and treatment of mental illness by Ayurvedic physicians.

Dr. Mukundan presented a comparative study of the clinical diagnosis of schizophrenic patients according to Ayurvedic and allopathic diagnostic criteria. Schizophrenic patients were classified according to the predominant imbalance of the Manodoshas and were rated using the PANSS (positive and negative syndrome scale).

Dr. Mukundan classified three subgroups of schizophrenic patients using the Kapha Pitta Vata Prakriti (personality) questionnaire. Schizophrenics diagnosed with a primary imbalance in Pitta showed a significant correlation with the positive syndrome scale on the PANSS. Schizophrenics diagnosed with a primary imbalance in Kapha showed a significant correlation with the negative syndrome scale on the PANSS.

A third group of schizophrenics was diagnosed with a primary imbalance in Vata; they were reactive and more difficult to treat. Using the Ayurvedic approach for clinical diagnosis, Dr. Mukundan identified this new subgroup of schizophrenic patients who were classified with a primary imbalance in Vata, were reactive, and whose symptoms were not correlated with the positive or negative syndrome scales on the PANSS. This study represents one of the first efforts to compare the clinical diagnosis and symptom profile of mentally ill patients using Ayurvedic and allopathic diagnostic criteria.



# Signs, Symptoms and Diagnosis of Mental Diseases in Ayurveda

R. H. Singh

Ayurveda is one of the most ancient systems of medicine in the world. Its antiquity goes back to Vedas, the oldest recorded wisdom on the earth. Ayurveda is essentially the science of life, health, and cure based on the eternal laws of nature. This unique ancient science has survived vividly through the ages and is flourishing today in new dimensions, attracting the attention of the world at large.

The authentic original knowledge about the science of Ayurveda is available in the form of two sets of Classic Sanskrit texts called *Brhatrayi* or three big books (*Charaka Samhita*, 600 B.C.; *Sushruta Samhita*, 500 B.C.; and *Samhitas of Vagbhata*, 600 A.D.) and *Laghutrayi* or three small books (*Madhava Nidana*, 900 A.D.; *Sarangdhara Samhita*, 1300 A.D.; and *Bhava Prakasa*, 1600 A.D.).

A review of Ayurvedic classics reveals that ancient Ayurveda was a highly developed medical science, and it was practiced professionally through its eight clinical specialties, hence called Astanga Ayurveda, namely, Kaya Cikitsa (internal medicine), Salya Tantra (surgery), Salakya Tantra (ear, nose and throat/ophthalmology), Kaumarabhrtya (obstetrics, gynecology, and pediatrics), Rasayana Tantra (geriatrics), Bajikarana (sexology), Bhuta Vidya (psychiatry), and Agada Tantra (toxicology). Thus, psychiatry finds a prominent place even in the ancient classical practice of Ayurvedic medicine.

It is pertinent to observe that psychiatry had its roots in Vedas where Bhuta Vidya finds vivid mention. The word Bhuta Vidya of Vedic texts refers to Ayurveda as a whole. There is no direct mention of Ayurveda, particularly its Tridosha doctrine (the three physical elements -Vata, Pitta, and Kapha), in Vedas. As such, Bhuta Vidya is the mother of medicine as a whole in ancient India.

Contemporary Ayurvedic psychiatry consists of two components: Ayurvediya Manas Roga Vijnana (rational Ayurvedic psychiatry)

and Bhuta Vidya (nonclassical Ayurvedic psychiatry in which the disease and its treatment are based on paranormal factors). Ayurvediya Manas Roga Vijnana deals with clinical conditions, where the disease and its treatment are based on fundamental principles of Ayurveda such as the theories of Pancha Mahabhuta (the five basic physical elements), Tridosha (the three bodily elements), and Triguna (the three mental elements) as in the case of Unmada (psychoses), Apasmara (convulsive disorders), Cittodvega (anxiety disorders), and so forth.

Bhuta Vidya deals with psychiatric problems like Bhutonmada (psychiatric syndrome or set of behavioral alterations named symbolically after a demon or supernatural being) and Grahavesa (psychiatric syndrome or set of behavioral alterations named symbolically after a planet or divinity), where the disease and its treatment are not based on classical principles of Ayurveda and its Yuktivijnana (rational knowledge) but rather on paranormal factors like the doctrine of Karma (actions of past life), Graha (spiritual force, planet, or divinity), and Bhuta (demons or supernatural beings). The latter appears to be more like astrology than psychiatry.

Some aspects of Bhuta Vidya are equated with demonology. However, on closer inspection, it appears that different kinds of Bhutonmadas and Grahavesas described in ancient texts are nothing but different forms of psychiatric syndromes or sets of behavioral alterations named symbolically after different Grahas because of the similarity with their mythological descriptions. Hence, the element of demonology exists only symbolically, not in reality, in Ayurveda.

## The Fundamental Principles

The entire concept of life, health, and disease in Ayurveda is derived from the classical theory of Loka-Purusa Samya (macrocosm-



microcosm continuum) which proclaims that the individual living being is a miniature replica of the universe and the Loka (Universe) and the Purusa (individual) exist as a continuum of each other. Ayu is the individual life entity which is four-dimensional, composed of physical, sensorial, mental, and spiritual attributes. The human being is provided not only with the Jnanendriyas (sense organs), but with a highly dynamic Manas (psyche/mind). According to Ayurveda, the Manas is highly active but is Acetana (unconscious). It derives its consciousness from the Atma (soul), which is an extension of the cosmic or divine consciousness. The consideration of the separate entity of the conscious element in this context is the uniqueness of Ayurveda and distinguishes it from Occidental thoughts and theories.

The Manas (the mind) is further considered three-dimensional in terms of the three Gunas (mental qualities) - Satva, Rajas, and Tamas. The Rajas represents activity and dynamism while the Tamas denotes inertia and darkness. Satva is the state of pure mind with absolute balance where both the extreme qualities of mind, namely Rajas and Tamas, cease or merge into each other. It is believed that all mental illnesses are due to the disorders of Rajas and Tamas. Satva is never the cause of illness. This is why Rajas and Tamas are also called Manas Doshas (mental elements) in the same way as Vata, Pitta, and Kapha are called the Sarira Doshas (bodily elements) and are associated with all kinds of physical diseases.

In consideration of the Trigunas, Ayurveda puts forward that there can be three broad categories of Prakritis (personalities), namely Satvika Prakriti, Rajas Prakriti, and Tamas Prakriti. On the basis of finer considerations, these 3 are further divided into 16 Manas Prakritis (mental traits). These 16 personality traits are characterized with unique features which may predispose the individual to specific mental diseases simulating the 16 personality factors of modern psychology.

The entire concept of Manas is psychological in nature. Its neurophysiological attributes have not been described in detail in Ayurveda. However, *Bhela Samhita* states that the Manas is located in the skull ontext.

(Sirastalvantar gatam Manah). There are also references describing Hridaya as the seat of Cetana (consciousness). This concept is controversial and need not be discussed in this context.

## **Mental Illness**

According to Ayurveda, mental health is a state of sensory, mental, intellectual, and spiritual well-being. Mental ill health (mental illness) is brought about essentially as a result of unwholesome interaction between the individual and his environment. This interaction operates through three fundamental factors, namely Kala (time, rhythm), Buddhi (intelligence), and Indriyarthas (sensory inputs).

Ayurveda believes in the theory of Punarjanma (rebirth) and Karma (actions of past life). Accordingly, the principal causative factors involved in mental illness are genetic factors, personality makeup, and environmental factors.

Mental disease in general is characterized by a wide range of altered behaviors. The clinical diagnosis is determined on the basis of the pattern of behavioral alterations and certain associated symptoms and signs. The common psychiatric diseases described in Ayurveda are different types of Unmada (psychoses), Apasmara (convulsive disorders), Cittodvega (anxiety disorders), Cittavasada (depressive illness), Mada (alcoholism and drug abuse), and Murcha and Sanyasa (conditions associated with coma).

Unmada as described in Ayurveda is the major psychiatric disease, which correlates broadly with psychosis as understood in Western modern psychiatry. Unmada (psychosis) is classified into subtypes which are identified in terms of the set of signs, symptoms, and the pattern of behavioral alterations referable to the three Doshas (elements)-Vata, Pitta, Kapha, and their combinations. It is possible to clinically correlate these subtypes of Unmada with different types of schizophrenia and other forms of psychosis such as manic depressive psychosis (bipolar disorder).

A separate category of Unmada Roga (psychotic diseases), which is described as



Agantuja Unmada (psychosis induced by external forces) by Charaka and as Bhutonmada (a psychiatric syndrome or set of behavioral alterations named symbolically after the name of a Grahas-planet or deity) by Sushruta, forms an interesting dimension of Ayurvedic psychiatry. Some scholars prefer to use the term demonology for this part of the knowledge. In this context, about a dozen psychiatric syndromes are described and named after different Grahas. The names of these Grahas seem to have been used symbolically to define particular sets of behavioral alterations that conceptually simulate the mythological descriptions of the respective Grahas. Thus, Bhutonmada is a specialized aspect of Ayurvedic psychiatry using symbolic terms and need not be considered in the realm of demonology.

### **Clinical Psychiatry**

Psychopathology in Ayurveda is described by Charaka in *Nidanasthana* Chapter 7 in a very systematic manner in terms of eight essential psychological factors which are considered to be centrally affected to varying degrees in all psychiatric disorders. The psychological factors are Mana (emotion, mood, affect), Buddhi (thought and decision), Sanjnajnana (orientation), Smriti (memory and learning), Bhakti (desire), Sila (habits), Cesta (psychomotor function), and Acara (conduct and behavior).

A review of the Ayurvedic texts reveals that a wide range of psychiatric conditions have been described. In addition to the etiology and pathogenesis, the texts describe briefly but vividly the signs, symptoms, and behavioral alterations in different psychiatric diseases and their classifications. The psychiatric conditions described in original texts may be classified as below.

1. Primary psychological conditions caused purely by the Manas Doshas (mental elements) Rajas (passion) and Tamas (inertia, lethargy): the Manas Dosha Vikaras (psychological illnesses) (C. VI 6:5).

Examples of the Manas Dosha Vikaras include Kama (lust), Krodha (anger), Lobha

(greed), Moha (delusion), Irsya (jealousy), Mana (pride), Mada (euphoria), Soka (sorrow, grief), Cinta (anxiety), Udvega (neurosis), Bhaya (fear), and Harsa (happiness).

2. Psychiatric conditions caused by a mixed Samprapti (pathogenesis) including both the Sarira (Vata, Pitta, Kapha) and Manas (Rajas, Tamas) Doshas.

Examples include Unmada (psychoses), Apasmara (convulsive diseases), Apatantraka (hysteria), Atatvabhinivesa (obsession), Bhrama (vertigo), Tandra (drowsiness), Klama (neurasthenia), Mada Murcha Sanyas (comas), Madatyaya (alcoholism), and Gadodvega (hypochondriasis).

3. Prakritis (personality disorders).

There are 16 Manas Prakritis (mental traits) which represent 16 types of behavioral traits. The Prakriti condition results from an overt imbalance in the Manas Prakritis accompanied by abnormal behavior and warranting psychiatric care.

4. Buddhi Mandya.

Mental retardation of varying degrees of primary or secondary origin.

5. Jara Janya Manas Vikara.

Psychiatric problems of the aged.

6. Manodaihika Vyadhis.

Psychosomatic diseases in which the cause of disease is mental and the manifestation is somatic. For example, Sokatisara (diarrhea of psychological origin).

7. Psychiatric syndromes named symbolically after the Grahas (planets or deities): Bhutonmada.

Bhutonmada warrants Daivavyapashraya Cikitsa (divine therapy) when Yuktivyapashraya Cikitsa (diet-drug therapy) is not effective.



## **The Psychiatric Examination**

In a psychiatric examination of a patient, the Ayurvedic physician pays special attention to the patient's environment, hereditary and genetic background, original personality makeup in terms of Tridosha (physical elements) and Triguna (mental elements) in addition to Dasavidha Pariksha (10 general methods of examination), mental stamina, lifestyle, and alterations in the above mentioned eight factors. In addition to the psychiatric examination, the patient is also examined in biological terms: Sadanga Pariksha (eight different methods of biological examination), including Srotas Pariksha (systemic examination) and Astavidha Pariksha (examination of all of the organs), which includes Nadi Pariksha (pulse reading).

The clinical examination in Ayurveda has a twofold objective: to examine and assess the primary nature of the patient as a human being and the state of his remaining health, that is, examination of the patient's health; and to examine and assess the nature and severity of the disease from which the patient is suffering. These two aspects of clinical methodology are called Rogi Pariksha (examination of the patient) and Roga Pariksha (examination of the disease), respectively. The Rogi Pariksha is done according to Charaka's Dasavidha Pariksha (10 general methods of examination), which includes Prakriti (constitution), Vikriti (morbidity), Sara (quality of tissues), Samhana (body build), Pramana (measurement), Satmya (adaptability), Satva (mental stamina), Ahara Sakti (digestive power), Vyayama Sakti (physical strength), and Vaya (age and aging).

The methodology used for clinical examination includes Prasna Pariksha (interrogation of the patient or a reliable informer) and Pancendriya Pariksha (physical examination of the patient). Pancendriya Pariksha consists of Astavidha Pariksha (eightfold examination or general survey of all of the organs) by Nadi (pulse), Mutra (urine), Mala (stool), Jihwa (tongue), Sabda (voice), Sparsa (skin), Drk (eye), and Akriti (facial expression or appearance); and Sadanga Pariksha (systemic examination of the six parts of the body) including the head-neck, trunk (chest, abdomen), and extremities along with

the 13 Srotamsi (channels) distributed over the Sadanga (body). The Srotas Pariksha (physical examination of the Srotas or Srotamsi) in the case of psychiatric patients must include the examination of Manovaha Srotas (pathways of the mind).

The clinical data are critically examined and evaluated in the light of the doctrine of Ayurvediya Pramanas Vijnana (knowledge obtained by observation and measurements) and Nidana Panchaka (fivefold etiology), namely, Nidana (etiology), Purvarupa (prodromal symptoms of a disease which appear during the onset), Rupa (characteristic signs and symptoms of a disease which appear when the disease is fully manifested), Samprapti (pathogenesis of a disease which consists of an interaction between Dosha-Vata, Pitta, Kapha and Dusya -local tissues), and Upasaya- Anupasaya (effects of drugs, diets, lifestyle on the disease). The diagnosis is made not merely by the name of a disease or syndrome but in a descriptive way identifying the Prakriti (mental constitution), Hetu (the cause of a disease), Vikriti (current state of disease susceptibility or morbidity), including Dosha (physical and/or mental elements), Dusya (seven basic tissues of the body which get vitiated by the Doshas during the disease), and Adhithana (seat of origin of the disease).

## **Principles of Treatment**

The management of a psychiatric patient in Ayurveda is done through three general types of therapy: Daivavyapashraya Cikitsa (divine therapy), Yuktivyapashraya Cikitsa (biological or diet-drug therapy), and Satvavajaya Cikitsa (psychotherapy). Daivavyapashraya Cikitsa includes the use of Mantra (incantation), Japa (chanting sacred incantations, meditation), other religious activities, and the wearing of precious stones. The Ayurvedic psychotherapy popularly known as Satvavajaya incorporates the principles of Asvasana (assurance therapy), replacement of emotions, and psychoshock therapy.

In Yuktivyapashraya Cikitsa, the patient is subjected to biopurification therapy by Panchakarma (fivefold internal purification and cleansing therapy; it consists of Vamana



(emesis), Virecana (purgation), Anuvasana Vasti (oleus enema), Asthapana (nonoleus enema), and Sirovirecana (nasal instillations) in order to cleanse the channels of the body, followed by Samsamana (palliative treatment) which uses Ausadhi (drugs), Anna (dietetics), and Vihara (lifestyle). The drugs used in Yuktiyapashraya Cikitsa are primarily Medhya drugs (CNS drugs which promote or are beneficial to the Medha-intellect, intelligence or memory promoting drugs, nootropic agents) or Medhya Rasayanas (CNS active substances or agents which promote or are beneficial to the Medha). Medhya drugs and Rasayanas are believed to act as brain tonics and adaptogens that afford a better mental health and lead to alleviation of the behavioral alterations. Bajikarana drugs (drugs used for promoting sexual stamina, virility, and fertility) such as Kapikacchu are used as mood elevators in the treatment of depression.

Ayurvedic management in its entirety is more health oriented than disease oriented.

As such, there is an emphasis on utilizing the Ayurvedic approach and therapeutics as an adjunct to the disease-oriented therapy of modern psychiatry to afford a full treatment.

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Now I shall describe the characteristics of Mahatatatwa. Chitta and mahatatatwa are one and the same. And in a subtle manner the entire universe is within Mahatatatwa, which is changeless, effulgent, peacefully and totally made up of Satwa. Now let us describe Ahamkar - the sense of separate self-hood. It has all the three gunas; it is the primal cause of indriyas, prana, antahkarana and devatas. It has peace, violence and dullness. And Mana is the ground from which all desires - sexual and others - emerge. It is characterized by thoughts and counter-thoughts. It is regulator of all Indriyas. Now let us describe Buddhi. Buddhi has knowledge about all substances and also the sensory perception is due to Buddhi. Buddhi is characterized by doubts, certainty, decision making, sleep and memory. And Shrotra (ears), Twak (skin), Chakshu (eyes), Rasana (tongue), Ghrana (smell), Vak (speech), Pani (hands), Pada (legs), Payu (ano-rectum) and Upastha/yoni (genital organs) are ten Indriyas. Their role is to be busy with their perception or work.

"Vachanamrit"

- Swami Narayana



# Assessment and Classification of Mental Disorders : The International Approach

M. K. Issac

The 1990s have witnessed new developments in the standardized assessment, diagnosis, and classification of mental disorders worldwide. For the first time in the history of modern psychiatry, we now have a common language in the field of mental health. Chapter V of the *Tenth Revision of the International Classification of Diseases* of the World Health Organization (ICD-10) deals with mental and behavioral disorders and is an essential component of this common language. A complete listing of standardized diagnostic assessment instruments and several lexicons which provide clear defini-

tions of terms complement the detailed description of mental and behavioral disorders in Chapter 5 of ICD-10. Chapter V also has linkages with the *Fourth Revision of the Diagnostic and Statistical Manual* of the American Psychiatric Association (DSM-IV). The current availability of vastly improved diagnostic criteria and assessment instruments should considerably reduce the international divergences of diagnosis of mental disorders. It should also promote transnational research efforts to improve the understanding of mental disorders and care of mentally ill patients.

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# Psychotherapy in Ayurveda

A. Praveen

As the world moves towards the 21st century with aspirations of continuous technological progress in ever-widening horizons of human achievements, an ancient medical system still survives in the Indian subcontinent catering to the health care needs of a vast majority of its population. A large section of humanity vigorously votes for a return to natural ways of life, and we find people all over the world coming together from time to time to exchange views on holistic approaches and their capacity as a medical system to respond to the call for a holistic system of healing.

Ayurveda, from its very existence, takes a comprehensive psychosomatic spiritual approach to all problems of health and disease with its twofold objective-, that is, prevention of diseases and alleviation of existing ones. In order to classify the disease on the basis of seat of illness, the diseases are grouped into two categories, namely, Saririka (physical) and Manasa (mental).

Ayurveda considers three important factors in the causation of both physical and mental diseases:<sup>2</sup> Asatmyendriyarthā Samyoga (unwholesome contact of sense organs with objects, incompatible physical, verbal, or mental activities), Pragnaparadha (volitional transgression), and Parinama (time factors including chronobiological errors, seasonal variations).

Charaka, while describing the causative factors of misery, gives a fair amount of importance to Pragnaparadha (volitional transgression). He says people whose Dhi (intellect), Dhriti (resolution, retention of information), and Smriti (memory) are impaired subject themselves to Pragnaparadha by virtue of their evil actions.<sup>3</sup> Intellectual pseudoconception and Improper conduct represent Pragnaparadha.<sup>4</sup> As intellect is the direct product of mind, this can happen only when the Manas (mind) is associated with its two Doshas (elements)-

Rajas (passion) and Tamas (inertia). Manas under the influence of these two Doshas cannot perform its normal function in this state; whatever perception is done by the sense organs leads to intellectual blasphemy.

Some examples have been considered by Charaka in the same context-<sup>5</sup> of life: forcible stimulation of natural urges and suppression of manifested ones, exhibition of undue strength, overindulgence in sexual acts, loss of modesty, enjoyment of harmful objects, avoidance of healthy activities, malice, vanity, fear, anger, greed, ignorance, bad actions arising out of any one of them, or other physically evil acts arising out of Rajas (passion) and Tamas (inertia). Each of these constitute Pragnaparadha (volitional transgression) leading to various ailments.<sup>6</sup>

Two other major causative factors of physical and mental diseases, namely, Asatmyendriyarthā Samyoga (incompatible physical, verbal, or mental activities) and Parinama (seasonal variations) may also come under the purview of Pragnaparadha; It is ultimately the Pragnaparadha that leads to these two causative factors.

Mind is known as Satva or Cetas. Its action is determined by its contact with its objects (like happiness or misery) and the soul. This acts as a driving force for all the sense faculties. The mind, object of the mind, intellect, and soul constitute spiritual elements and qualities. They serve as factors for prompting an individual to indulge in or refrain from virtuous and sinful acts.

Performance of an action, that is, a therapeutic action, depends upon the material object-<sup>8</sup> The sense faculties together with the mind get vitiated by Atiyoga (excessive utilization), Ayoga (nonutilization), and Mithyayoga (wrongful utilization) of the objects concerned. This causes an impediment to the respective sense perception. If correct utilization of the sense faculties is restored, the respective sense perceptions return to normalcy.<sup>9</sup> Thinking constitutes the



object of mind. So the proper utilization, Atiyoga (excessive utilization), Ayoga (nonutilization), and Mithyayoga (wrongful utilization) of the mind or mental faculty is responsible for normal or abnormal mental conditions.<sup>10</sup>

It seems that this etiological consideration is more related to the preventive aspect and is too gross to understand the nature of the illness and plan its management. Though the causes of some particular mental disorders are specifically mentioned in the classics, it is not very easy to interpret them to suit our present needs. In regard to pathogenesis, the Ayurvedic classics mention that the disturbance of the equilibrium of the Manasa Gunas (qualities of the mind, Rajas, Tamas, Satva), predominance of the two Manasa Doshas (mental elements) -Rajas (passion) or Tamas (inertia), or reduction in Satva Guna causes mental disorders.<sup>11</sup> Such disorders are relatively minor. When the somatic Doshas (elements), Vata, Pitta and Kapha, are involved in the pathogenesis, the diseases produced as a result of such an interaction are considered to be major physical disorders.

Regarding the clinical aspect, Charaka precisely mentioned that Unmada (psychosis) results from the derangement of eight principles, namely Mana (mind), Buddhi (intellect), Sanjnanana (orientation and responsiveness), Smriti (memory), Bhakti (desire), Sila (habits), Cesta (psychomotor activity), and Acara (conduct). Although Charaka considers these principles only for Unmada (psychosis),<sup>12</sup> clinically it appears that these are applicable to all cases of mental illness. However, the nature and type can vary in individual illness.

The method of treatment in Ayurveda as a whole has been classified into three categories by Charaka.<sup>13</sup> Daivavyapashraya Cikitsa (spiritual therapy), Yuktivyapashraya (rational or diet-drug therapy), and Satvavajaya (psychotherapy).

Daivavyapashraya Cikitsa (spiritual therapies) include incantation of Mantras, use of a talisman, wearing of gems, auspicious offerings to God, gifts, oblations, observance of scriptural rules, atonement, fasts, chanting of auspicious hymns, obeisance to god, and going on a pilgrimage. Administration of proper diet and medicinal drugs comes under the second category. Withdrawal of the mind

from harmful objects constitutes psychotherapy.

Daivavyapashraya Cikitsa (spiritual therapy) is not currently as popular as the other two strategies. This is because sufficient work has not been done for proving its usefulness. If visualized properly, all the modes of treatment used in this type of therapy are aimed at Santvana (assurance) and are helpful in regaining the lost confidence in a patient. Therefore, there is a very thin line of demarcation between this type of treatment with Satvavajaya Cikitsa (psychotherapy) because both are nonpharmacological modes of treatment aimed at correcting an imbalanced state of mind. The word "Daiva," in *Atharvaveda*, refers to the acts of the past life. Therefore, Daivavyapashraya Cikitsa (spiritual therapy) is designed to exhaust evil acts of the past and thus combat the Daivikrita diseases (diseases caused by evil acts of the past) by providing assurance to the patient with a different mode of approach.

In Yuktivyapashraya Cikitsa (diet-drug therapy), the treatment is based on reasoning and necessary planning. The causes of diseases are determined, and suitable ways and means are devised to effect a cure based on fundamental principles of Ayurveda-Pancha Mahabhuta (the five basic physical elements), Tridosha (the three physical elements), and so forth. The pathogenesis is eliminated by administering appropriate medicines and by prescribing a suitable diet. Both Yuktivyapashraya Cikitsa (diet-drug therapy) and Satvavajaya Cikitsa (psychotherapy) lines of treatment go hand in hand for a complete recovery in a mental disease.

Just as Ayurvedic physicians found a rational therapy for the treatment of somatic diseases in Yuktivyapashraya Cikitsa (diet-drug therapy), they have also found it essential to have a line of treatment that is specific to mental diseases. Accordingly, it was to be based on normalizing the Manasa Doshas (mental elements). Similar to the Tridosha theory related to physical disorders, Ayurveda says that Nidana Parivarjana (identification and avoidance or elimination of the causative factors of a disease) accounts for half of the total therapeutic measures.<sup>14</sup> Thus, Nidana Parivarjana is essential for the



successful management of both Saririka (physical) and Manasa Rogas (mental diseases).

The aim of Satvavajaya Cikitsa (psychotherapy) is to **augment the Satva Guna** in order to correct the imbalanced state of Rajas (Passion) and Tamas (inertia). Charaka was the first person to use the word Satvavajaya. He defines it as a method of restraining the mind from Ahita Arthas (unwholesome objects). Unfortunately no further description of Satvavajaya Cikitsa (psychotherapy) is available in Charaka Samhita. The word is mentioned only once in his text, and the applied aspects of this method of treatment are not described.

All of these facts reflect one thing-psychotherapy including Satvavajaya was done by some specialists at the time of Charaka. References are available to prove the above presumptions. Charaka advises that people should go to specialists for such treatments. "Manasam Prati Bhhaishajyam Trivargasyanvavekshnam, Tadvaidya seva vijnanamatmadinam Cha Sarvasha".<sup>15</sup>

The following are to be considered in the treatment of Manasa Roga (mental disorders): to attend to the course of conduct relating to Dharma (virtue), Artha (wealth), and Kama (desire); to render service to the persons wellversed in the nature and cure of Psychological diseases; and to obtain all-round knowledge about the self.

In Astanga Hrdaya, while explaining the ideal therapies of mind, Vagbhata says Dhi (discrimination), Dhairya (courage, strong Will), and Atmadi Vijnana (knowledge of the self) are the ideal ones.<sup>16</sup> Again, in Charaka Samhita while explaining the principles of treatment for Manasa Rogas (mental disorders), the following opinion is given:<sup>15</sup>

A wise person should very carefully consider again and again what is useful and what is harmful for health; he should strive for discarding the harmful or unwholesome regimens and adopt the wholesome ones in regard to Dharmna (virtue), Artha (wealth), and Yama (desire), for no happiness in this world can occur without these three elements.

Therefore, one should try to serve persons well-versed in the nature and cure of Manasa Rogas (mental disorders). One should also try

to acquire knowledge of the self, the place, family, time, strength, and capacity. Satvavajaya is a typical Ayurvedic approach which not only prevents the impairment of intellect, patience, or memory, but also brings them back to a normal state, if they are impaired. Thus, Satvavajaya plays a significant role in the maintenance of a harmonious state among these three important factors, ultimately leading to a happy, healthy state of the individual.

Normally, mind including the Artha (wealth), Buddhi (intellect), and Atma (soul) remains undisturbed. In order to maintain their balance, one should make all efforts to maintain their normal condition. This can be achieved by the performance of duties after duly considering their pros and cons with the help of intellect, and with the sense faculties applied to Hita Arthas (their respective wholesome objects). This can be achieved by acting with consideration to the qualities of place, season, and one's own constitution, including temperament. So one who is desirous of his own well-being should always perform noble acts with proper care. Hence, one who observes these principles simultaneously fulfills both the objectives-maintenance of positive health and control of the sense faculties. To fulfill this, one has to follow the Sadvritta (right conduct) described by all authors. A few of them are considered here.<sup>17</sup>

One should pay respect to Deva (God), Go (cow), Brahmana (priests) and Guru (preceptors), Vridha (elderly people), Siddha (those who have accomplished spiritual perfection), and Acharya (teachers). One should offer oblation to the fire and wear good herbs. One should perform Sandhya (a Vedic ritual to be performed at dawn and dusk), take food after the digestion of the previous meal in limited quantity, and not initiate urges of the body by force. All human activities are meant for the happiness of all the living beings, and such happiness is based on Dharma (virtue, doing good acts), hence every person should adopt Dharma. One should avoid tensions pertaining to the body, speech, and mind such as Himsa (causing injury or torture), Steya (stealing), Anyatakama (unlawful sexual activity),

Paisunya (abusive or harsh speech), Anrita



Vacana (scolding), Sambinna Alapa (speech causing dissension), Vyapada (quarreling, intention of hurting), Abhidya (jealousy, not tolerating the good of others), and Drigviparyaya (finding fault, misunderstanding). One should help Avritti (people who have no means of livelihood), Vyadhi (people who are suffering from diseases), and people who are afflicted with grief. Even the insects and ants should be treated with compassion and kindness. One should be very helpful to others even though they are not helpful. "Sampadvipatsu ekamana heta virsyate naphalenatu"-one should maintain a balanced mind during wealth as well as during calamity. One should be envious of the cause but not be jealous of the effect. One should speak appropriately to the occasion, with words which are good and pleasing. One should initiate conversations with a pleasant face; be virtuous, kind, and mild; not be comfortable and happy alone; make others also like oneself, and neither believe nor suspect everyone. Keeping in mind the nature of other people, one should deal with them in a manner pleasing to them. The sense organs should neither be strained very much nor coaxed very much. One should not engage oneself in occupations which are devoid of the three pursuits-Dharma (virtue), Artha (wealth), and Karma (actions of past life).

One should wear precious stones, potent hymns (verses with meaning), and herbs on the body. This reminds one of the Daivavyapashraya Cikitsa (divine therapy). Some of the following phrases should also be practiced: Kruddanamanupeta-reconcile the angry, Bheethanam asvasayita-console the frightened, Dheenanam abhyupapatte -be merciful to the poor, Satya sandhah-be truthful, Paraporushavacana Sahisnu-be tolerant toward incompatible words uttered by others, Am-Arsagna-be in control of intolerance, Prasama guna darshi- be of peaceful disposition, and Raga dwesha hethunam hanta cha-conquer the very roots of attachment and hatred.

The main aim of all these Sadvritta<sup>18</sup> (right conduct, good acts) is to increase Satva Guna (quality of the mind) and to mitigate Rajas (passion) and Tamas (inertia) Gunas. One who adopts these codes will surely attain long

life, health, wealth, reputation, and also the eternal world.

While explaining the treatment for Unmada (psychosis), Charaka says that if mental derangement is caused because of loss of something which the patient loved, then he should be made to regain a similar object.<sup>19</sup> "Istadravya vinasattu mano yasyopahanyate tasyatatsadsya prapti santvasou samamnayet". Simultaneously, he should be consoled with pleasing assurances as a result of which he becomes free from the ailment. If Unmada is caused by passion, grief, fear, anger, exhilaration, jealousy, and greed, then the exposure of the patient to mutually contradictory emotions will cure the ailment. Further, he continues, the patient should be consoled by friends with religious and moral statements. They should announce the loss of something which the patient loves or exhibit surprising events. Fear or psycho-shock therapy is another important method of treatment which can be included in Satvavajaya Cikitsa (psychotherapy). In principle, it is very much similar to the electroconvulsive shock therapy which is used in modern medicine.

In the definition of Satvavajaya, the word Manonigraha means control of mind. This mind control can be both subjective and objective. Self-control of the mind is one of the most difficult tasks and warrants a perfect combination of desire, determination, and dedication. It can be achieved as Lord Krishna concludes in Bhagavad Gita<sup>20</sup> "Abhyasena tu kounteya vairagyena ea grihyate, that is, by practice and detachment". This sort of mind control can be included in Yoga and hence seems different from the Satvavajaya (psychotherapy) that Charaka has described. The objective type of Manonigraha (mind control) mentioned in Ayurveda is the actual Satvavajaya Cikitsa (psychotherapy) and warrants the physician's interference to control the patient's mind. However, the subjective type of Manonigraha (mind control) can be achieved by different sources explained in Sadvritta and also by following the yoga.

Hathayoga Pradipika compared the mind with mercury and says that if these two can be controlled, the impossible becomes



possible,<sup>21</sup> and only the mind can control the mind, and for this a lot of patience and practice is required.

According to Upanishadic tradition, yoga is a higher state of consciousness which is achieved when the activities of the five senses and the fluctuations of mind are stilled and the Buddhi (intellect) becomes steady-Yoga citta vritti nirodha.<sup>22</sup> According to Patanjali, yoga is a state of Citta Vritti Nirodha or a state of controlled mind. Citta Vritti (Vishayakara) means fluctuations of the mind around the world of objects. Such fluctuations of mind are considered to be in five categories: Pramana (the three fundamental ways of knowing or measuring-direct perception, inference, and textual testimony), Viparyaya (one of the two different kinds of fluctuations of mental being), Vikalpa (one of the two different kinds of fluctuations of mental being), Nidra (sleep), and Smriti (memory). According to Patanjali, such Vrittis (fluctuations of the mind) can be taken care of by Abhyasa (intense study) and Vairagya (renunciation). "Abhyasa vairagyam tannirodhah"<sup>23</sup>-the effort to divert the Vrittis toward the path of detachment and renunciation-is termed Abhyasa, and the attempt to stop such a flow of vrittis and the attitudes of mind is termed Vairagya; this can be achieved by practicing Pranayama. In *Tejabindupanishat*, Pranayama has been explained as "Nirodhah sarva vrittinam pranayama." Even Pratyahara can help in this regard; in *Mandala Upanishad*,<sup>24</sup> it is stated that "visayebhya indriyrthebhyo manonirodha pratyaharah," meaning Pratyahara is a process of mental control and withdrawal of the mind from sensory functions.

Hence, Manonigraha (mind control), as explained in Satvavajaya Cikitsa (psychotherapy), can be achieved even with the help of yoga. *Patanjala Mahabashaya* also signifies the same.<sup>25</sup> With the help of an eminent Vaidya (physician), the patient will be able to control his mind by different methods. It may

be more useful to healthy individuals because they will be in a better position to appreciate the objectives. Persons with minor mental derangement may also be able to understand and adopt these measures. But gross involvement of the mental faculty warrants a very different approach.

Discussions related to Satvavajaya Cikitsa (psychotherapy) are scant, brief, and nondescriptive in the Ayurvedic literature and hence, in a way, ineffective to attract public attention. There is an increasing need to review and revitalize the concepts of Ayurveda in the better interests of science and society at large. Satvavajaya Cikitsa needs further analysis and processing and has to be presented in a more practical and acceptable way.

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" Personal attributes are psychic symbols. We may consider these symbols the genetic material of our psychological identity. As the genes code for the structural proteins of the cell, these self-symbols transcribe our personal ground plan, our character armour... the process and content of the questioning unfolds along the character lines of the previous identity. The physician may serve as target sounding board, or ignoramus in this mental exercise of the restoration of identity".

- Joseph R. Glaser



# Pharmacotherapy and Psychotherapy: Differential Impact on Symptoms and Outcome?

R. C. Casper

"Healing is not a science, but the intuitive art of wooing nature."

W.H. Auden  
*The Art of Healing*

Psychotherapy and pharmacotherapy are two forms of wooing nature into healing the mind. The two treatments are not necessarily antithetical, since the mind is naturally anchored in the brain, and body and brain form part of the same living human organism.

Too little is known about the subtle early genetic and environmental changes and vulnerabilities which precede psychological and psychiatric disturbances to develop targeted interventions. For optimal growth, the human infant requires not only adequate nutrition, but adequate and benign human physical and emotional contact which then, through sensory and psychological stimulation, channels the brain's timed genetic program and postnatal development.

Albeit the specifics of the process cannot as yet be traced scientifically,<sup>1</sup> it is assumed that this sensory, cognitive, and emotional input influences programmed neuronal death, helps phenotypically diverse neurons organize into functional units and to become interconnected through the formation of specific axonal and synaptic contacts, and hence modulates the maturation and growth of neurotransmitter systems and generates neuronal circuits that underlie individual human behavior, not only in childhood, but throughout life.<sup>2</sup>

Maturation, just as therapy, is a reciprocal process in that the infant's emotional and physical responsiveness and engagement provide and invite feedback to its caretakers. The acquisition of language is a good example of this interaction, since speech will not develop without auditory stimulation from dialogue and exposure to language in human company.

Emotional neglect and early faulty or

impaired maternal or caretaker transactions can, as the pioneering studies of Spitz<sup>3</sup> in orphaned infants have shown, lead to depressive withdrawal and a high mortality rate. Harlow and his coworkers<sup>4</sup> have demonstrated the devastating long-term effects of maternal absence on monkeys' social and sexual adolescent and adult development. Both sets of observations suggest profound and enduring neurobiological alterations if sensory and emotional input are impaired or missing.

Ayurvedic medicine offers an outstanding example that as long as mankind has designated people as healers, both psychotherapy and pharmacotherapy have been applied to mental disturbances. Psychopharmacology and psychotherapy redress the impairment induced by the psychiatric disorder on different levels, the first through chemical agents, the second through psychological means.

Research in chemistry and pharmacology has identified the active substances in many natural drugs along with their mechanism of action at the molecular level. The establishment of the FDA in the United States in the 1950s led to Government regulation of drugs. Proof of safety and efficacy is now required before a new drug can be launched. Interestingly, although with the introduction of psychoanalysis some ingredients in the therapeutic relationship have been conceptualized, the practice of psychotherapy remains essentially unregulated.

The purpose of this chapter is to compare treatment efficacy of pharmacotherapy and psychotherapy for the two major psychiatric syndromes, schizophrenia and depression. How convincingly has research validated either one of these treatments or both in combination as effective or ineffective? Do each show specific action?

In view of our lack of knowledge about the causes of mental disorders, clinical studies have tested the efficacy of traditional and dual



newer therapies through their ability to alleviate symptoms, to arrest the progression of the disease, to restore the individual to previous levels of function, and to prevent relapse through maintenance therapy and through teaching new coping strategies.

**Pharmacotherapy-Psychotherapy  
Goals of Treatment**

- Cure: restore to health or to previous level of functioning
- Symptom alleviation
  - specific behaviors are the targets of changes
  - accelerate the healing process
- Arrest progression of the disease process
- Acquire new ways of coping
  - relapse prevention with maintenance treatment

The healing process traditionally can be divided into three parts:

- The self-healing properties of the body (the natural course of the disease).
- Changes induced by nonspecific effects (placebo, psychological treatments).
- Specific effects of physical or pharmacological interventions (surgery, radiation, drugs).

**The Placebo as a Form of Treatment**

Since all helping interventions share the so-called placebo effect, its recognition as part of any treatment is important. We first consider the significance of the helping relationship and the literature on the placebo effect.

Placebo (I shall please) action is defined as "the psychological, physiological or psychophysiological effect of any medication or procedure given with therapeutic intent. 5 Considered a contaminant of research, the placebo has become an important component of conventional drug research design. By requiring double-blind placebo-controlled studies, the FDA acknowledges the power of

the doctor-patient relationship and of any substance dispersed or technique applied. Furthermore, the notion of the placebo washout, the intent to exclude placebo responders during the first week or two from entering drug trials, reinforces the notion of the healing action of the placebo. Any medical treatment can, and probably does, function as placebo.

Two requirements are necessary for a placebo effect to occur: the disease process itself or the symptoms must be capable of variable intensity, both over time and in different patients, and there must be a doctor-patient relationship, actual or implied. Placebo effects vary in different individuals and in any one person at different times. Evaluation of the true placebo effect, that is, the pharmacology of placebos, controlling for dose, timing, administration route, and possible side-effects, requires inclusion of an untreated (placebo treated) control group in randomized clinical trials. The true placebo effect is highly variable but can be significant and has been documented in studies of the introductory placebo washout. 7 8

**The Placebo in General Practice**

- In 40-60 percent of patients attending general practice, no firm diagnosis could be made.
- In the United States after 1950, psychological illness tripled and in the United Kingdom, psychological illness more than doubled between 1955 and 1971.
- 40-50 percent of patients expected to be given a prescription, whereas doctors thought 80 percent or more of patients wanted a prescription.

Source: Thomas<sup>6</sup>

Improvement of depressive disorders with placebo administration has been linked to a short illness, depression of moderate severity, a precipitating event, and surprisingly, a good response to previous antidepressant treatment.

One recent study, after many fruitless attempts to identify a placebo responder personality, reports that volunteers with Type A personality characteristics, that is, competitive and hostile traits, reported significantly



Proportion of patient population who reported measurable improvement after 4-6 weeks of treatment in controlled studies

	Placebo	Specific drug
Schizophrenia	0-10%	60-90%
Obsessive-compulsive disorder	10-20	35-50
Bipolar disorder, manic	10-20	60-90
Depressive disorders	20-45	60-75
Anxiety states without depression	60-65	60-90
Headaches, angina pectoris, postoperative pain, back pain	15-58	30-80

Source: Beecher;<sup>9</sup> Laporte<sup>10</sup>

more adverse effects from taking placebo than volunteers with a Type B personality.<sup>11</sup> Regarding such nocebo effects, a large-scale phase I study reported adverse events in 19 percent of healthy volunteers. Complaints were more frequent after repeated dosing (28 percent) and in elderly subjects.<sup>12</sup> Nocebo effects can be frankly toxic, for example, angioneurotic edema has resulted from placebo therapy.<sup>13</sup>

## Psychotherapy

Since the modern management of depressive disorders relies heavily on the use of medication, a question important to ask—given the labor-intensive nature and high cost of psychological therapies—is what kind of changes in psychopathology can we expect from psychological therapies? Other reasons for examining outcomes from psychological treatments are that psychotropic medications are no panacea, given their side-effects, which in the case of the antipsychotic drugs can be debilitating and irreversible. Finally, the safety profile of the psychotropic drugs in pregnancy is unknown. There is a need for alternative treatments which could help a troubled mother and protect the fetus from drug exposure.

Psychotherapy might offer a place for self-examination and reeducation to improve the

self-concept, psychosocial function, or interpersonal skills. Has psychotherapy been shown to be effective, and what are its specific indications?

One of the problematic issues, especially in psychotherapy research, centers around the difficulty of stimulating a "no contact" condition, since patients who receive minimal contact or "psychotherapy on demand" may not perceive themselves as getting no therapy. Each form of psychotherapy differs in some elements of its philosophy, yet each provides patients with a plausible system of explanations for their difficulties and with principles that seek to guide future behavior. Expressed differently, one might say psychotherapy acts through understanding the patients' communications and behavior, then interprets the patients' experiences with the aim of influencing and changing their thinking, attitudes, and behavior. The assumptions underlying psychotherapy are shared by all psychological treatments and may be implicit in the drug treatment condition.

Psychotherapy is not for everyone. There has to be an ability and willingness for self-examination and self-reflection. Of course, cultural factors may not be conducive to psychotherapy. Individual psychotherapy, an

Psychotherapy is based on the assumption—

- That personal relationships are crucial to human maturation and individual development.
- Of the unconscious—one of Freud's significant contributions. Only a small part of our mind is at any one time accessible to conscious awareness and self-reflection.
- That much of our behavior and feelings are not consciously controlled and are subject to the influence of automatic processes.
- That in neurosis or psychosis, ideas, thoughts, images, feelings, and sensations which are normally kept out of consciousness enter awareness, not necessarily in an orderly or intelligible fashion.



outgrowth of psychoanalysis, puts a high premium on personal relationships. Cultures where family or society values outrank individual needs might prefer group therapy. Women might be more suited to psychotherapy than men, given women's naturally greater verbal endowment and tendency to socialize.

Psychotherapy presupposes an ability to-

- Establish a personal relationship (therapeutic alliance) which is experienced as benevolent and beneficial.
- Enter voluntarily into a therapeutic relationship and to reveal oneself.
- Process information and to increase self-control over thoughts / feelings / behaviors.
- Collaborate and cooperate.

Age has been said to be a limiting factor. Older people might be too set in their ways for psychotherapy to have an effect, and cost is a consideration. So far, there are only a handful of studies on psychotherapy for depression in the elderly. A recently initiated NIMH study underway since 1991 investigating psychotherapy for the elderly is said to cost \$30,000 per patient.<sup>14</sup>

The empirical data on the outcome and efficacy of psychotherapy are vastly outnumbered by the empirical data on the efficacy of drug treatment. Since it is beyond the scope of this chapter to present a complete review of all studies, let alone compare methodological differences between studies, representative studies were selected to answer the questions posed in the title.

### Pharmacotherapy

Antidepressant and antipsychotic medication are hypothesized to correct deficiencies in various neurotransmitter systems and as a result help reestablish control over thoughts and ideas or reequilibrate mood states. In practice, since the etiology and the basic mechanisms underlying the disordered thought or mood are unknown, improvement is measured as behavioral or symptomatic change.

It is well known that Delay and Deniker's

### Pharmacotherapy

- Directed at a specific disorder or symptom
- Scientifically documented efficacy and safety
- Established side-effect profile
- Mechanism of action can be studied independently
- Requires compliance with taking recommended drug in recommended dose

report<sup>15</sup> in 1952 describing the antipsychotic action of chlorpromazine grew out of a serendipitous observation by Laborit, who had set out to synthesize antihistamines with greater sedative properties in order to enhance anesthesia during surgery. This discovery of the specific antipsychotic effects of the phenothiazines turned out to be the cornerstone for drug development in the treatment of schizophrenia. At the same time, the antidopaminergic action of chlorpromazine provided a heuristic model for abnormal brain in schizophrenia. Other antipsychotic drugs such as the butyrophenones were then developed in quick succession.

Seeman<sup>17</sup> has identified the dopamine D2 as one of the crucial antipsychotic/dopamine

### Psychotropic drugs recommended for psychiatric disorders in 1969

Disorders	Drugs
Schizophrenic disorders, including childhood schizophrenia; other delusional states	Phenothiazines Butyrophenones Reserpine
Depressive disorders	Tricyclic compounds MAO inhibitors Phenothiazines Barbiturates
Manic disorders	Phenothiazines Butyrophenones Lithium carbonate
Organic brain disorders	Phenothiazines Psychostimulants

Source:WHO Scientific Group<sup>16</sup>



receptors, because antipsychotic drugs exhibit dissociation constants at the D2 receptor that correlate well with the antipsychotic action of oral doses. In depression, such a correlation between the drugs action at the receptor and the clinical effects is much weaker. For example, there is no evidence that links the blockade of serotonin reuptake to antidepressant efficacy or the potency of blocking serotonin reuptake to antidepressant potency. In point of fact, a French antidepressant (tianeptine) that enhances serotonin reuptake is equally effective as an antidepressant.<sup>18</sup>

### **Design of Reviewed Studies**

This section gives an overview of the current information on the comparative effectiveness of pharmacological and psychological treatments and the specific action of each approach in schizophrenia and depression. For the most part, the reviewed studies were controlled inpatient, and in depressive disorders, mostly outpatient, trials that evaluated the efficacy of drug treatment in comparison with psychological treatment or a combination of the two relative to placebo and a no-contact control. Not all include placebo as reference treatment. The studies span 30 years and differ in design, yet certain fundamental research requirements are met by all. Methodological differences between these and other studies and how they affect comparability and validity are discussed in greater detail by others.<sup>19-21</sup>

### **Sample**

The subjects cover the full adult age range and include both male and female patients. Most schizophrenic patients were young adults, and most depressed patient were in their thirties and forties. Subjects were recruited based on explicitly stated inclusion and exclusion criteria. Study populations invariably reflected a select group, since they consented to participate and were willing and able to cooperate and collaborate. Attrition and dropout rates varied from 20 to 35 percent of patients entered into studies.

### **Diagnostic Criteria**

Diagnoses were determined according to

criteria outlined in the diagnostic classification in use at the time of the study.

### **Assessments**

The use of standardized rating scales for evaluating illness severity, global functioning, baseline symptoms, and symptomatic change was the rule, even in the early studies. The instruments rated target behaviors or symptoms expected to change. In fact, some of the earlier studies collected a wealth of information from nurses, therapists, trained raters, the patients, and other observers.

### **Study Duration**

Study length varied from 6 weeks to 4 years. Depending on the time course of change, the shorter duration might have been insufficient to allow for change in the condition.

### **Treatment**

Pharmacological treatment consisted of one drug given in a constant or flexible dose, close to but not always the maximum dose. Psychological treatments varied considerably. Treatment for schizophrenia could include individual, family, group, or supportive therapy, multiple families therapy, social skills training, or psychoeducation. Individual psychotherapy, with focus on cognitive restructuring and interpersonal function, was the preferred mode of treatment for depressive disorders. In most early studies, large numbers of mostly experienced psychotherapists carried out individual therapy, drawing on their own expertise and taking a flexible approach. In more recent studies, a manual that described the theoretical underpinnings of the approach, general strategies involved, and suggestions for dealing with specific problems was used to carry out therapy following manual-based training of not always experienced therapists.

## **Results**

### **Schizophrenia**

The results of research by May,<sup>22</sup> Grinspoon and associates,<sup>23</sup> and other investigators in the late 60s and early 70s



demonstrated, as May put it, "beyond reasonable doubt that ataraxic (antipsychotic) drug therapy is the most effective single form of specific treatment for schizophrenic hospital patients and also the cheapest." Drug treatment was shown to lead to improvement in a significantly higher number of schizophrenic patients than any other treatment, including psychotherapy. When drugs were combined with psychological treatment, a slight advantage over drug treatment alone was observed (table 1).

The improved abstraction and greater insight with psychotherapy observed in May's study<sup>22</sup> reflected general and not disease-specific effects. Psychotherapy alone was ineffective in schizophrenia. Following the publication of this indisputable evidence, antipsychotic drug treatment remained the mainstay for treating schizophrenia to which psychological treatments were added. The introduction of the antipsychotic drugs led to an exodus from state hospitals of schizophrenic patients who were discharged home to their families or into community living. Medication compliance was found to be crucial for any form of psychological treatment even to take place. Braun<sup>19</sup> concluded that a supportive outpatient milieu was as effective as hospital treatment for all but the most acute patients, again only if patients remained on medication.

The next question regarding the duration of treatment and the benefits of intermittent drug treatment or a drug "holiday" have only recently been conclusively answered with the observation that relapse rates were significantly reduced by drug maintenance as opposed to intermittent medication.<sup>24</sup> Herz and associates proposed an early intervention approach where patients who have experienced previous schizophrenic episodes are taught to recognize prodromal signs of relapse, such as insomnia, tension, anxiety, or withdrawal. If patients, upon recognizing these symptoms, increase the dose of their medication, they apparently require less hospital treatment than those simply maintained on medication. Early recognition of first onset cases and early intervention with medication is currently being investigated in Europe and the United States.

Hogarty and his group<sup>25</sup> and others<sup>26</sup>

continue to devote considerable effort to tailoring psychological treatment to the needs of schizophrenic patients. It is conceivable that some features inherent in psychotherapy are not quantifiable, such as the acceptance and tolerance of patients' needs and vulnerabilities which relieve their despair and demoralization and might reduce suicide rates, which occur at a rate of 10 percent in untreated schizophrenic patients. The design of the studies does not permit a test of the influence of psychological treatments on the quality of life of schizophrenic patients.<sup>27</sup>

Social skills training and family psycho-education markedly reduce relapse rates. However, just as in the case of drugs, the gains are lost if these psychological treatments are discontinued. The superiority of multiple family versus single family therapy in lowering relapse<sup>28</sup> might well be related to a reduction in pathological family affect and style of interaction, since Vaughn and Leff<sup>29</sup> have shown that the affective tone or expressed emotion of the family affects the course of schizophrenia. There is awareness that the long-term treatment of schizophrenics requires highly effective interpersonal skills, and Hogarty<sup>25</sup> has proposed a kind of personal therapy which accommodates the underlying psychopathology. Forty years after the discovery of the antipsychotic action of chlorpromazine, the psychological treatment of the schizophrenic patient is still alive in more than one approach, but there is no longer any doubt that psychological treatments have little power to improve the core symptoms of schizophrenia.

### **Depressive Disorders**

The information from well-designed clinical trials on the comparative efficacy of drug treatment versus psychotherapy suggests that pharmacotherapy is by far the most effective treatment for depressive disorders, except in cases of mild to moderate depression where psychotherapy seems to be equally beneficial or might be more effective. However, both placebo and cognitive or interpersonal psychotherapy offer symptom relief and can bring about remission in depressive disorders (table 2).<sup>30-33</sup>

There is some evidence that the anti-depressive effect of psychotherapy takes using



**TABLE 1.** Schizophrenia: Treatment outcome from pharmacotherapy, psychotherapy, family and group therapy

Diagnosis	Age	N	Sex	Treatment	Tx length	Results	Study
Schizophrenia	16-45	228	F 51% M 49%	1. Trifluoperazine 2. Individual psychotherapy 3. Both 1 and 2 Combined 4. Electroshock 5. Conservative care	6-12 mo	Most effective: Drug alone, Drug + psychotherapy Psychotherapy alone, n.s., Cost 3x drug treatment Combined Tx: improved abstraction and insight	22
Schizophrenia chronic and acute	18-35	20	M 100%	Thioridazine + psychotherapy; placebo + long-term intensive psychotherapy; periodic placebo washout	2-4 yr	Drug and psychotherapy sig superior in improving psychotic symptoms and behavior Psychotherapy had no effect	23
Schizophrenia	30-40	1500	---	Controlled trials of alternative to hospitalization	Review of studies	Supportive outpatient treat- ment equivalent, sometimes superior to hospital Tx; all on medication	19
Schizophrenia schizoaffective	19-60		M 51% F 49%	Intermittent drugs maintenance antipsychotics	2 yr	46% relapse; intermittent drugs 14% relapse, maintenance drugs	24
Schizophrenia	mean 27	103	M 66% F 34%	Social skills training (SST) Family psychoeducation (FT) Medication alone	1/wk-1 yr 2/mo-2 yr	SST & FT 20% relapse SST > FT = 1 year SST < FT = 2 year patients remained impaired	25
Acute psychosis Schizophrenia	18-45 mean 19	172	M 74% F 26%	Multiple and single family groups, individual psychotherapy, all medication	2 yr	Cumulative relapse rate: multiple family group 16% single family group 27% Medication compliance 65%	28



**Table 2.** Treatment outcome from controlled studies comparing psychotherapy versus pharmacotherapy in depressive disorder

Diagnosis Study	Age	N	Sex	Variable	Psychotherapy	Control	Pharmacotherapy	Results	
Depression	25-60	106	F	SAS	Added to TCA, if better: 8 mo maintenance	Placebo	TCA, AMI 100-150 mg	8 MO: Psy: work performance ↑ interpersonal communication ↑ anxious ruminations ↓	33
Major depressive disorder	18-65	81	F 85% M 15%	SADS, Raskin, Hamilton	16 weeks interpersonal	Waiting, could telephone	TCA, AMI 100-200 mg	AMI: sleep appetite ↑ Psy: interest, mood, suicidal ideation, work ↑ AMI + Psy: best outcome	30
Major depressive disorder	30s	44	F 61% M 39%	Beck Hamilton Hopelessness scale	12 weeks cognitive		TCA, IMI 75-250 mg	Cognitive superior to IMI; ↓ hopelessness; ↑ self-concept; 1 yr followup: cognitive superior	34
Pathological grief	30s	18	F (1 M)	Symptoms on dynamic ratings	12 sessions	---	---	12/12 symptomatic change could be rated; neurotic conflict ratings little agreement	42
Major depressive disorder	30s	75	F 75% M 25%	Beck, Hamilton, Raskin, MMPI, SAS	2/w cognitive 12 weeks	Placebo .05 mg atropine, 5 mg phenobarbital	TCA NORT 50-150 mg	Cognitive therapy as effective as medication; combined treatment no additive effect; 40% no better	43
Major depressive disorder	mean 35	155 162	F 70% M 30%	Beck Hamilton Hopkins, GAS	16 weeks, 1/w cognitive-interpersonal	Placebo and clinical management	TCA, IMI 150-200 mg + CM	IMI + CM best; psychotherapy next best; reanalysis: in less severely depressed patients, no difference among treatments Predictors: Interpersonal: ↓ social dysfunction; Cognitive & IMI: ↓ cognitive dysfunction;	31 37

Continued



**Table 2.** Treatment outcome from controlled studies comparing psychotherapy versus pharmacotherapy in depressive disorder

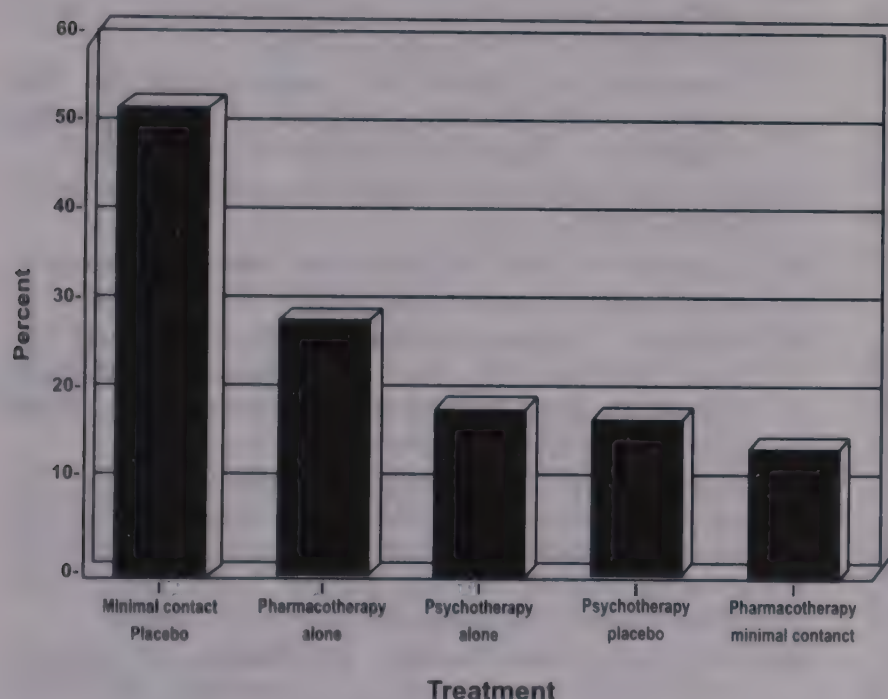
Diagnosis	Age	N	Sex	Variable	Psycho-therapy	Control	Pharmaco-therapy	Results	Study
Major depressive disorder	21-65	128	F 82% M 18%	Hamilton, Raskin, GAS	3 yr maintenance interpersonal	inter-personal + placebo	TCA, IMI 150-300 mg	IPT + IMI 131 weeks; IMI 124 weeks; IPT 82 weeks; Placebo 45 weeks; interpersonal focus monthly session prophylactic	38

Abbreviations : TCA: tricyclic antidepressants  
 IMI: imipramine  
 AMI: amitriptyline  
 NORT ?  
 SAS: Social Adjustment Scale  
 MMPI : ?

SADS : Schedule for Affective Disorders and Schizophrenia  
 Beck: Beck Depression Inventory  
 Hamilton : Hamilton Depression Inventory  
 Raskin: Raskin Mood Scale  
 GAS : Global Assessment Scale  
 Hopkins:



longer when compared to medication, about 4-8 weeks, or can only be detected after long-term (8 months) treatment. Psychotherapy has been shown to have a beneficial effect on self-concept, mood, and apathy and leads to better social functioning and work performance when contrasted with drug treatment.<sup>32-34</sup> Antidepressant drugs improve physiological parameters, such as appetite and sleep, the so-called endogenous components of depression, early on, during the first 1 to 2 weeks of treatment.<sup>30 35 36</sup> The NIMH Collaborative Treatment of Depression study,<sup>31</sup> in design and sample size most suited to explore these issues, concluded that the findings provided only "scattered and relatively insubstantial support for specific differences" between psychotherapy and pharmacotherapy.<sup>37</sup> The best treatment outcome for depressive disorders is achieved if medication is combined with psychotherapy.<sup>20</sup>



Percent evidence for the superiority of combined psychotherapy pharmacotherapy for depressive disorders over comparison conditions<sup>20</sup>

Higher quality psychotherapy as defined by greater focus on specific personal problems, such as marital disputes or interpersonal deficits, was associated with a longer delay in the recurrence of depression as opposed to less focused interpersonal psychotherapy.<sup>38</sup> By and large, judging by the changes in mood or behavior, antidepressant drugs seem to act swifter in arresting the pathological process

underlying the depressive illness and maintain patients for longer periods in remission.

## Discussion

The treatment studies in depressive disorders do not easily lend themselves to an analysis of differential treatment effects nor to an estimation of the quality of the improvement. For the most part, the assessment instruments were selected to measure the amount of change. The Beck and Hamilton depression scales are included in most studies under the assumption that these scales consist of one principal depression factor which is scored and reported as a number, but the scales are rarely scrutinized for change in a single symptom. Only studies that did include specific rating instruments, such as the social adjustment scale, or those that explored the influence of treatment on specific symptoms did report differential effects.

That the topic remains of empirical interest is confirmed by recent investigations that have examined the relationship between biological indices and psychotherapy. For instance, hypercortisolism in depressive disorder has been found to be associated with a less adequate response to cognitive therapy.<sup>39</sup> In a sleep study, Thase and colleagues<sup>40</sup> identified a particular sleep EEG profile-reduced REM latency, increased REM density, and poor sleep continuity-as a predictor of a poorer response to cognitive and interpersonal psychotherapy. Although patients with this sleep constellation tended to be older, the investigators believed that this profile was not simply an epiphenomenon of age or clinical severity. Taken together, the findings support the view that young in patients with milder depressions do well with psychotherapy.

Given new drug developments, it is conceivable that new drugs, in action similar to the selective serotonin reuptake inhibitors (SSRIs), might replace psychological treatments in mild depressions. To our knowledge, no comparisons between psychotherapy and the effects of SSRIs have been published.



Lastly, the observations of Schwartz<sup>41</sup> that psychological treatment, such as behavior therapy, can bring about measurable and identifiable changes in brain metabolism provide sound evidence that psychological treatments have a demonstrable impact on brain function.

### Conclusions

- There is no definitive study in the literature which settles the question of comparative worth of psychotherapy versus pharmacotherapy.
- Research studies that have compared pharmacotherapy to psychotherapy have focused for the most part on quantifying symptomatic change and on measuring rates of relapse and recurrences, and not measuring treatment-specific effects.
- In schizophrenia, antipsychotic drug treatment reduces positive, and less so, negative symptoms during the psychotic episode; drugs accelerate recovery and effectively prolong remission from psychotic episodes. Psychological treatments ease the patient's adaptation to the disorder, promote drug maintenance, help the family, and serve to alert the patient to the prodromal signs of psychosis.
- For depressive disorders of sufficient severity to impair functioning, antidepressant drugs are the treatment of choice. In milder depressions, interpersonal and cognitive therapy effectively ameliorate the depression, improve apathy, social effectiveness, work performance, and marital relationships. Placebo effects, pharmacotherapy, and psychotherapy all change similar core symptoms, and each can lead to full recovery from depressive disorders.
- Finally, new studies, and these hopefully will include Ayurvedic medicines, need to be designed to explore the effectiveness, specificity, duration, and prophylactic effects of psychological treatment relative to drug therapy. The studies should also address the question to what extent medication or psychotherapy can improve the patient's quality of life and resourcefulness.

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# Ayurvedic Approach to Mind and Mental Diseases

**N. V. K. Varier**

An overview of psychotherapy implies an estimation of the present advances along with tracing the various turns it had taken in its progress. A study of the limitations and achievements of the past and how we can utilize such a study guides us to improve our present practices and to tackle the current problems facing us. For this, studies related to psychotherapy in Ayurveda are also necessary.

The status of psychotherapy is very high now. It is always dependent on psychology. Today we have a plethora of psychologies, and it is said that the coming century is to be an era of psychology. We talk about explosion of knowledge. Every branch of knowledge has something to contribute to psychology. The approach to universe and man is the source of psychological attitudes. Earlier, we have passed through stages in history in which our understandings were formed and guided by totemism, magic, and religion. So corresponding mental attitudes also progressed.

Since the beginning of the present industrial era, objective study of matter based on analysis has become important. We have advanced various studies on mind also. We already hear of many trends such as empiricism and behaviorism. This era started with the declaration of Descartes that mind and body are two compartments. This statement is radically different from the approaches so far followed in earlier studies.

As the focus of advancement turned toward the biological as well as social sciences from inert sciences like mathematics, physics, and chemistry, the old approaches came back but with a higher scientific vision and understanding. Two basic trends appear to have advanced—one directed to psychology, psychoanalysis of Freud, Jung, and their followers, and the second based on experimental studies of the higher nervous system such as those of Sechenov, Pavlov, and others prove that mental activities are higher physiological

activities in which mind and body are inseparably integrated. Studies by both approaches have helped to promote psychotherapy. But practical experiences and findings in laboratory experiments have proved that Descartes' approach is misleading, and what helps to promote science is the approach that takes body and mind as inseparable.

Experiments in higher spheres of science endorse this approach. For instance, it is reported that parts of the body which we designate as physical have mental aspects as well, and what we call mental has physical roles also. White corpuscles which were relegated to the role of guardianship to fight foreign bodies are now reckoned as parts of the moving brain itself. Likewise, it is said that if the current sphere of research in genetics is on the role of DNA and RNA, in the coming era, it is going to be on informational molecules. We see the emergence of new branches of science such as psycho-neuroimmunology. All these developments point out that the scientific world is now heading to a holistic approach. It is on this background that we have to evaluate the significance of the present workshop.

How can we fully utilize the contributions of science for the benefit of mankind? It is acknowledged that to promote science, we need planning. Study of past experiences is equally important as new discoveries and inventions for planning. All the traditional systems present us the recorded experiences. So repossession of our ancient wisdom, as Doctor Raymond Obosowin captioned the paper presented at the International Conference on Traditional Medicine (organized by IDRC in Ottawa, Canada, March 1994), is the slogan of the day.

Particularly, the experiences of traditional medicines in India and China are more valuable because these nations are old civilizations. The studies of recorded experiences of Ayurveda have undergone reviews c,



and modifications periodically in the light of ever-advancing knowledge that had originated in our country and abroad. Professor Needham, in the introduction to his monum-ental work *Science and Civilization in China*, explains the motto that prompted him to take up this work. He points out the fact that up to 13 centuries after Christ, the flow of science was from the East to the West. The science and knowledge advanced here is with the outlook of a functional universe, an outlook which the West is now obliged to accept after 300 years of scientific materialism. So, the experience of Ayurveda, which has also advanced with a functional, holistic, and field-oriented approach, is a valuable treasure for science.

In India, as in all other countries, the origin of the medical system can be traced to the remote past and has advanced through outlooks of Totemism, magic, and religion and was later raised to the status of science. The term Ayurveda (science of life) came into vogue with the composition of the *Samhitas*, like *Charaka*, *Sushruta*, *Kasyapasamhita*, and others about 600 B.C. Ayurveda of that era had attained such a position that it embraced all medically useful outlooks, understanding, experiences, and techniques up to that time. Ayurveda has undergone revisions and modifications accepting new studies and assimilating without shedding its own principles, and this process has been there at all stages of the renaissance in the past and in present times also. *Charaka* speaks of three approaches of medicine: *Daivavyapashraya Cikitsa* (based on divinity, divine therapy), *Satvavajaya Cikitsa* (based on conquering the mind, psychobehavioral therapy), and *Yuktivyapashraya Cikitsa* (based on rationalism, diet-drug therapy). *Daivavyapashraya* is the form of treatment in the *Vedas* and *Tantras*. All diseases, physical or mental, are *Badhas*-afflictions from extraneous agents. They are to be driven out by magical rituals such as prayers addressed to the gods, medicines, herbs, jewels, talisman; all of these act because of their magical power. But many of the medicines and techniques that later entered into Ayurvedic texts with new explanations have their origins from these sources. Along with it and as a part of *Tantra*, *Satvavajaya*

(psychobehavioral) methods also were in practice, that is, controlling the mind and body by yoga, meditation, and similar techniques to strengthen the mind to withdraw from sensual pleasures, unwholesome foods, and ways of life to protect one from diseases.

*Yuktivyapashraya* (rationalistic, diet-drug therapy) medicine is the Ayurvedic approach. It is based on the study of the *Loka* (universe) and *Purusa* (man) as constituted by materials formed by five *Mahabhutas*, that is, *Pancha Mahabhuta* (five basic physical factors or elements making up the mind, body, and the universe), each *Mahabhuta* having specific properties, and substances representing the sum total of the *Mahabhuta* properties. The *Loka* and *Purusa* are always in motion, that is, in transformation. Health is in the accord of man with changing conditions and diseases due to discord which upsets the balance of functional factors in the organism and creates imbalance that leads to disease. So treatment is to restore that balance.

To restore the balance, substances are used as treatments based on the properties and actions of their *Mahabhutas*. There are 20 *Gunas* (material properties or attributes; 10 pairs of opposing attributes) inherent in the *Mahabhutas*: heavy, light, slow, fast, cold, hot, unctuous, dry, smooth, hard, dense, amorphous, soft, rough, stable, unstable, subtle, gross, transparent, and opaque. In physiological and pathological studies, the *Tridosha* concept is used to diagnose and treat diseases. Anatomy and physiology in Ayurveda are mainly based on the *Tridoshas*. Each organ of the body contains a balance of the *Doshas* (physical elements, *Vata*, *Pitta*, *Kapha*). The functions of the organs are determined by the *Doshas* and by influencing the *Doshas*. So although the Ayurvedic approach is objective, it is different from the approach of modern medicine in which properties are primarily dependent on the structure of cells, organs, systems, and so forth.

The rationalistic Ayurvedic approach is a continuation advanced and modified under the influence of new developments. The old approach of magic and *Satvavajaya* is a functional approach to mind and universe. Gradually, more information and experiences



from structural studies as in Sushruta were developed. By this period, the Darsanas were developed. It was a period of renaissance.

The Darsanas-Samkhya, Yoga, Nyaya, and Vaishesika -are based on and directed by studies of the phenomenon with its material bases. The Tridosha theory of Ayurveda evolved from the new studies with new visions. Charaka says that many medical systems were in vogue at the time and that Ayurveda emerged from them. It emerged in a period of renaissance with a higher vision, with objective studies but also functional. Ayurveda retained many practical and useful aspects of older medical disciplines but was modified by the rationalistic approach.

The Samkhya theories in Charaka present the Purusa as a conglomeration of 24 principles, as a picture in which man represents the universe. Accordingly, in Ayurvedic physiology the mind and body, which are not separate, are the seats of diseases. Bhavaprakasa presents their relationship as analogous to the container and the contents of the vessel, ghee. If ghee is heated, the vessel also is heated, and when the vessel is heated, ghee melts naturally.

Charaka says that the root of all diseases is in the mind. Misguided actions are offenses committed to intelligence, termed Prajnaparadha (volitional transgression), or actions by the mind and body violating the rules of nature and virtue (social duties). Blocking and straining the urges of the body such as the urge for belching, farting, defecation, urination, sneezing, thirst, hunger, sleep, coughing, gasping, yawning, crying, vomiting, and discharge of semen are the Prajnaparadhas (volitional transgressions) of the body.

Indifference to paying respect to those who deserve it, such as the elders, teachers, higher personalities, and to places of worship, as well as immoral acts, stealing, violence, desire for another's property, and committing similar sins are Prajnaparadhas (volitional transgressions) committed by the mind. Men are led to such misguided attitudes because of the infatuations or fallacies of the mind. Satva (purity), Rajas (passion), and Tamas (inertia) are the three Gunas (properties of the mind). Satva is unblemished goodness,

Rajas is action and brightness, and Tamas is inertia and darkness. The latter two are also referred to as Manas Doshas (mental elements) because they get vitiated by attachment to sensual pleasures.

When Satva (pure consciousness) is strong and Rajas (passion) and Tamas (inertia) are subordinate, no disease occurs. When Rajas and Tamas predominate, inappropriate and excessive desires lead to Prajnaparadhas (volitional transgression). Considered in this way, the mind is the root of all diseases, Mental and physical.

Yoga is fixing the mind in Satva (pure consciousness). When studying psychosomatic constitutions, this aspect is important. Mental qualities are dependent on the Prakriti (personality), and Prakritis are classified according to the Doshas (physical elements). There are seven types of Prakritis (personalities). The best Prakriti is the one in which all of the Doshas are equal-Samadhatu Prakriti. A man with Samadhatu Prakriti can control the mind, excitation, and inhibition. The second best is Kapha Prakriti, in which inhibition is strong and is one with tolerance, power, and Satvik qualities. The Pitta Prakriti is more prone to excitation but strong. Vata Prakriti is weak, melancholic, with weak power for excitation and inhibition. Prakritis with two Doshas are the worst. Thus, the physical constitution designated by the Doshas also determines the mental nature.

Both somatic and mental diseases are caused by the same factors-continuous use of unwholesome food, recourse to wrong ways of life, and violation of the rules of nature and society. Each Dosha (element) is vitiated and provoked by the specific nature of food and habits which create properties similar to that of the Dosha. Treatment is aimed at restoring the lost balance of the specific properties of the Doshas in their increased or decreased states from normalcy. So the condition of the Doshas is important and how we can restore normalcy is also important. For this, one has to scrutinize various factors such as the affected tissues, the site of disease, the strength of the patient, seasons, the state of the digestive fire, temperament, age, tolerance, power, adaptabilities of the patient, and all other related conditions. A decision is then made regarding the type of treatment. If



the Doshas are in excess and the patient is strong enough, the first preference is purification of the Doshas in both physical and mental diseases. Otherwise, pacification is employed, and Rasayana (restorative remedies or tonics) techniques are preferred. This is the general rule of treatment.

The difference between a somatic disease such as fever and mental diseases such as Unmada (psychosis) and Apasmara (epilepsy), is that in the former the upset Doshas (elements) affecting the physical conditions at first, create mental abnormalities later, while in mental diseases the vitiated Doshas in the mind affect the body later.

The various types and conditions occurring in a somatic disease, such as fever, and its relationship with mental factors will be reviewed. Agantuja (fever due to extraneous agents) is one of the eight types of fever. Agantuja itself is divided into four subtypes: induced by Grahas (spirits or deities) or resulting from a reaction to drugs, poisons, or mental agitations due to anger, fear, sorrow, or sexual desire. Jwara (fever) is classified as somatic fever and mental fever even though the basis of the disease is in the stomach. The course of treatment and the methods relating to the prescriptions in fever are used as guidelines for the treatment of all diseases either somatic or mental. The only specialty in fever is that the stages of treatment are different.

In fever and other somatic diseases, the first phase is generally the Ama stage (a state in which the Srotas (channels of the body) are blocked leading to an accumulation of Doshas). This stage is resolved by the use of reducing treatments that are appropriate to the causative Doshas (elements), such as fasting with mild emesis in Kapha type fevers; dehydrating and taking only a little hot water in Vata and Kapha type fevers; and medicated water with cooling and digestive herbs in Pitta type fevers. These are followed by lightening treatments such as fomentations (hot compresses containing herbs), allowing time for digesting Ama (toxins), serving gruels only, medicines, diet with bitter or pungent tastes, and others. Then only gruels and Kashayas (decoctions) are given. The aim is to resolve the Ama state.

In the second stage, treatment is done to

promote the strength of the body after the purification and pacification. This is employed by the intake of medicated ghees. Purgation is indicated in the debilitated patient-serving medicated milk. Then decoctions and unctuous enemas, errhines, inunctions, fumigations, and blood-letting are all prescribed according to the causative Doshas (elements) and stages of the disease. How to handle fevers induced by mental agitation is described as well. In fevers induced by Grahas (spirits or deities), magical rituals such as Balis (oblations or offerings) and Mantras (incantations) are used. The fever created due to anger is to be counteracted by provoking desire. Similarly, the fevers due to fear and sorrow are to be counteracted by desire and anger, respectively. In this way, the fevers due to mental agitation are counteracted. Thus, in the treatment of fevers, we have a guide for studying the stages and how techniques and medicines are administered according to the causative Doshas, stages, troubles, and so forth.

There is no specific categorization of mental and physical diseases in Ayurveda. Among the eight branches of Ayurveda, some mental diseases come under Grahavignana (psychiatry) and others come under Kaya Cikitsa (general medicine). Diseases such as Balagrahas and Bhutas (psychiatric syndromes named symbolically after the name of a Graha -planet or deity, or Bhuta-spirit, demon), Unmada (insanity), Apasmara (epilepsy), and Atatvabhinivesa (obsessions) are considered to be mental diseases, while Mada (intoxication), Murcha (syncope), and Sanyasa (coma) are considered to be psychosomatic diseases. In all these diseases, the mind is affected due to the vitiation of the Doshas (mental or physical elements).

The concept of Graha (illness induced by extraneous agents such as demons in children and adults) is a continuation of the old approach of the Veda. Texts declare it as taken from Atharva Veda. In Ayurveda, the treatment of Graha-induced illness has undergone a change. Ayurveda has incorporated the Dosha concept while retaining the old approach and techniques. So, medicines and methods aimed at counteracting the Dosha conditions are prescribed and magical



performances to expel the devilish forms and bodies that are believed to have affected the patient are also allowed,

Ayurvedic texts describe illnesses induced by Bhutas (demons, spirits), Grahas (planets, deities), and such bodies as illusions of the mind. When extraordinary or super-human features are seen in a person's understanding, speech, or actions, the person is said to be affected by the Bhutas. The person affected by Bhuta imitates the form, nature, speech, and actions of the model of the Bhuta's body or form in his mind as phantoms. But Charaka says that in truth, there are no such bodies. No Deva (god), Pisacha (goblins), Gandharva, or Rakshasa are there. We create Chidra (split in our mind) due to Prajnaparadha (volitional transgression). It is in this state that we feel affected by Graha. Eighteen types of Bhutas are described in *Astangahridaya* according to the models that are imitated. Balagrahas, although said to be induced by a Grahas created by Lord Shiva (constituting five males and seven females), are diseases with convulsions and phobias.

Unmada (psychosis) and Apasmara (epilepsy) are induced by similar factors that vitiate the body and the mind together. Factors include unwholesome food, Prajnaparadhas (volitional transgression), and others. Individuals who have low mental vitality (Hinasatva), are overwrought with sorrow, are weak due to diseases or to events that upset the mind, or have ingested poisons are affected. These factors cause the mind to become upset, and if the Manavahasrotas (channels of the mind) are blocked, Unmada (insanity) results. In this condition, because of the illusion of intelligence, knowledge, and memory, the affected individual, having lost all sense of happiness and pleasure, roams with no object, as a chariot without a charioteer. Apasmara (epilepsy) causes havoc to memory and occurs in individuals whose minds are harmed by over-thought, sorrow, and fear. The impurities in the body and mind destroy Satva (vital mental power) and pervade the mind and channels which carry action impulses. As a result, the affected individual falls into darkness, becomes stupid, and commits disgusting actions.

The following description gives a general

idea of the approach, principles, and methods used to deal with psychiatric diseases. Unmada (psychosis) is divided into six types due to an imbalance in each of the three Doshas (elements) separately, a combined type with all of the Doshas together, and two other types caused by sorrow and poisons. Apasmara (epilepsy) is divided into four types caused by each of the Doshas singly and by all of the Doshas combined. Unmada is a disease that continues, whereas Apasmara is episodic. In Unmada, Manavahasrota (mental channels) are blocked, whereas in Apasmara, memory is attacked and the channels that carry the action potentials are blocked. In both of the diseases, the aim of the treatment is purification of the mind.

Purification is done by Panchakarma (fivefold purification therapy) in which internal and external oleations (oil treatments) are the first step. In these cases, oleation with medicated ghee (prepared with herbs and animal products that are particularly good for tranquilizing the mind and cleansing) are given first. The ghees are selected according to the causative Doshas (elements). For instance, Ghritas (medicated ghees) such as Kalyanaka, Mahakalyanaka, Paisachika, Mahapaisachika, and Brahmi Ghrita are given.

In Unmada, all purificatory treatments along with fumigation and inunction (application of an ointment containing herbs), which are suggested in the context of treating fever due to mental agitation, are performed. Consoling, threatening, and arousing passions opposite to the causative passions are all employed. In Apasmara (epilepsy), the first attempt is to awaken the memory by removing the block. All purificatory steps from emesis, errhines prepared with the bile of animals, and others are done using acute medicines. Continuous intake of Panchagavya Ghrita, Brahmi Ghrita, and Kusmanda Ghrita; use of errhine medicines; inunction (massaging) of oils; and fumigations with such preparations are suggested. But as Apasmara is a disease which affects the Mahamarma (vital human mind) by provocation of the Doshas of the mind and body, it is a longstanding disease. In such situations, the advice is to resort to Rasayana (rejuven-



medicines, one must try to improve the mental condition by a sympathetic approach. The preceptors advise thus, "do not tell the patient that he had been doing disgusting actions when he had been unconscious. On the other hand, try to please his mind with words and things that cheer him."

In psychosomatic diseases such as Mada (alcoholism), Murcha (fainting), and Sanyasa (syncope), the treatment is directed against the cause and stage. In alcoholism, instead of suddenly stopping the drinking, gradual withdrawal is suggested. Small quantities of alcohol with medicines are given. In Sanyasa (syncope), the coma stage is met with emergency steps to awaken the consciousness using errhines (medicines promoting nasal discharge, secretion) with acute medicines, and so forth. In Mada and Murcha, the treatment is the same as that used for the combination of Vata and Pitta type of somatic illness.

To summarize, all diseases, psychic or physical, are caused by more or less the same provocation of vitiated Doshas (physical and mental elements). In mental diseases, the Doshas primarily affect the mind, Manavahsrotas (mental channels), and channels of action impulses connected with this. The aim of treatment is purification of the mind by the proper steps. Yogas and techniques that are

more helpful to purify the mind are prescribed. For longstanding diseases, Rasayana (restorative remedies or tonics) techniques are followed. Generally, herbs such as Vaca (*Acorus calamus*), Brahmi (*Bacopa monniera*), Jatamansi (*Nardostachys jatamansi*), Satavari (*Asparagus racemosus*), Sankhapushpi (*Clitoria ternatea*), Visala (*Citrullus colocynthis*), Nagadanthi (*Baliospermum montanum*), Thriphala (*Thri myrobalans*), and the use of animal products such as the urine of cattle are employed for treatment purposes.

It is difficult to categorize herbs, animal products, and minerals as medicines for mental diseases alone. All medicines that purify the body create mental tranquility also. Even fruits such as ashgourd or spices like ginger are recommended for use. Kusmanda Ghrita, a medicated ghee prepared mainly with ash gourd, is recommended for mental diseases. Ginger with jaggery is a medicine for many somatic conditions; it is also used for improving physical and mental stamina. Purification is the aim of the treatment. For this, a holistic approach is followed. Kerala special treatments, such as Dhara, Pizhichil, Talam, and others are very effective in tranquilizing patients and improving mental health.



# Clinical Trials Carried Out at the Ayurvedic Research Unit (C.C.A.A.S.)

M. G. Ramu

Ayurvedic treatment of diseases consists of three main components: Ausadha (drugs), Ahara (diet), and Vihara (nonphysical measures). Each has a distinct role to play in disease management. They bestow a cure when used in judicious combinations. Therefore, it becomes worthwhile to examine the role of each of the components in the treatment of different disease conditions.

The Ayurvedic unit at NIMHANS has conducted several pilot and controlled studies for assessing the efficacy of herbal drugs documented in the Ayurvedic classics and popularly used by Ayurvedic practitioners throughout the country in the management of different types of Manovikara (psychiatric illnesses). Three controlled studies and one pilot study are presented here.

## Use of Brahmyadiyoga and Tagara in Acute Schizophrenia

In a double-blind controlled study carried out by Mahal and colleagues,<sup>1</sup> the efficacies of the herbal drug Brahmyadiyoga, chlorpromazine (CPZ), and placebo were compared in patients with Unmada (acute schizophrenia). Brahmyadiyoga consists of six ingredients: whole plant juice of Mandukaparni (*Centella asiatica*), rhizome powder of Vaca (*Acorus calamus*), root powders of Jatamansi (*Nardostachys jatamansi*), Tagara (*Nymphoides macrosperrum*), Kushta (*Saussurea lappa*), and Sarpagandha (*Rauwolfia serpentina*).

One hundred and thirty-six patients with acute schizophrenia were selected for the study. The subjects were of either sex between the ages of 16 and 45 years. Twenty-eight subjects subsequently dropped out of the study. Twenty-seven patients were assigned to each of the four treatment groups. Stuporous and excessively withdrawn patients were not included in the study. The duration of illness varied from 2 months to 2 years.

The psychiatric diagnosis was made in accordance with the National Institute of Mental Health collaborative study of phenothiazine.<sup>2</sup> The Ayurvedic diagnosis was made on the basis of Lakshanasamuchaya (signs and symptoms) and Manahkarma (function of mind). The psychiatric assessment was made on the basis of the psychotic symptoms rating scale.<sup>3</sup> The Ayurvedic assessment was based on an examination of Manas (mind), Buddhi (judgement), Sanjnanana (orientation and responsiveness), Smrti (memory), Bhukti (desire), Sila (habits and temperament), Cesta (psychomotor activity), Acara (conduct), and symptoms present or absent in the patient. The assessments were done at the beginning of the trial and repeated every 2 weeks.

The psychological assessment using a multiphasic questionnaire and a spiral aftereffect test (SAET) was done initially and after completion of the treatment.

Brahmyadiyoga, Tagara, and placebo (8 g, 12 g) were administered in four divided doses, and CPZ (200 mg, 300 mg) was administered in a single dose during the first and second months, respectively. All the medicines were given in identical sugar-coated tablet form. Routine blood and urine examinations were carried out before and after treatment.

Based on the psychiatric assessment, the following observations were made: the mean effectiveness of Brahmyadiyoga was better than that of placebo; the mean effectiveness of chlorpromazine was better than that of Tagara; the mean effectiveness of Brahmyadiyoga was not significantly different from that of CPZ; and the difference between the mean effectiveness of Tagara and placebo was not significant.

Based on the Ayurvedic assessment, the following observations were made: Brahmyadiyoga was better than placebo; CPZ was better than placebo; and no significant differences were found between the other treatment groups-Tagara versus Brahmyadi-



yoga, Tagara vs. placebo, Tagara vs. CPZ, or Brahmyadiyoga vs. chlorpromazine.

Based on the psychological assessment, the following observations were made. The data from the multiphasic questionnaire failed to show any significant difference in the degree of improvement among patients in different treatment groups. This may be because the scoring method used in the analysis was not adequate for a before and after assessment. However, the analysis did show a tendency for patients to improve in the CPZ and Brahmyadiyoga treated groups. The results of the SAET showed that the maximum improvement was obtained in the chlorpromazine treated group. The difference in other treatment groups was not significant.

No side-effects were observed in any of the treatment groups. No differences were found in the laboratory investigations of the three groups.

The objective of the present study was to find out the effectiveness of the single drug Tagara and the compound drug Brahmyadiyoga in patients suffering from acute schizophrenia (various types of Unmada). CPZ was found to be significantly superior to Tagara and placebo. The overall effect of CPZ was found to be better than that of Brahmyadiyoga, but the difference was not statistically significant.

Improvement in the mental condition of the patients treated with Brahmyadiyoga was significantly greater than in patients treated with either Tagara or placebo. The general practice in Ayurveda is to use a combination of drugs in both physical and mental disorders. As observed in this study, the single drug Tagara exerted a favorable antipsychotic action on the patients. However, it was not as effective as Brahmyadiyoga. The possible explanation for this difference is that a single drug may not be as effective as a compound drug in normalizing all of the mental functions and resolving the imbalance of Doshas (mental elements). As expected, the patients treated with placebo did not show much improvement. The failure to find a difference in SAET in the Brahmyadiyoga treated group may be because the interval between the initial and final assessment was too short and the sample used for analysis was small.

### **Use of Brahmyadiyoga in Chronic Schizophrenia**

In a double-blind controlled study carried out by Ramu and associates,<sup>4</sup> the efficacy of Brahmyadiyoga was compared with CPZ and placebo in patients suffering from Anavonmada (chronic schizophrenia). Seventyeight patients of either sex, suffering from schizophrenia with a chronicity of 2 to 8 years were selected for the study. Thirteen patients dropped out of the study. Of the remaining patients, 23 received Brahmyadiyoga, 22 received CPZ, and 20 received placebo.

The psychiatric diagnosis was done using the ICD-9 (International Classification of Disease-9).<sup>5</sup> The Ayurvedic diagnosis was based on signs and symptoms of Unmada and the Ayurvedic mental status examination.

The psychiatric assessment used the psychotic symptoms rating scale.<sup>3</sup> The Ayurvedic assessment was based on the examination of Mana (mind), Buddhi (decision), Sanjnajnana (orientation), and other signs and symptoms present or absent in the patient.

The psychiatric and Ayurvedic assessments were done before starting the treatment, on the 31st day, and just after the completion of treatment on the 76th day.

The following tests were carried out before and after completion of the treatment: reaction time, critical flickerfusion threshold, vigilance test, and Fergusell's behavior rating scale.<sup>6</sup> The drugs were given as detailed below in four equally divided doses in the form of identical sugar-coated tablets. The duration of treatment was 75 days.

The psychiatric assessment was done at

Treatment	Brahmyadiyoga	CPZ	Placebo
Days 1-30	12 g	300 mg	12 g
Days 31-75	16g	450 mg	16 g

the end of the treatment period. According to the symptom rating scale, CPZ was significantly better than Brahmyadiyoga and placebo on the total score in the middle assessment. In the final assessment, CPZ was also significantly better than Brahmyadi- the initial and final score on the Rockland



yoga and placebo. both in the negative and positive scores. In addition, the change over time with each treatment was studied by comparing the initial and final score on the Rockland Scale. There was no significant reduction in any of the total, positive, and negative scores in the placebo group. At the other extreme, in the CPZ group, there was a highly significant reduction ( $P<.001$ ) in total and positive scores. The Brahmyadiyoga group registered a moderate reaction of positive scores, while the total and negative scores remained essentially the same.

The psychological assessments indicated that both Brahmyadiyoga and placebo groups did not show significant differences between their initial and final performances on the psychological tests.

In six patients in the Brahmyadiyoga group, nausea and vomiting developed toward the later part of the trial, and one patient developed jaundice (hepatotoxicity). One patient in the CPZ group had intense thirst throughout the trial period. No remarkable changes were noticed in the blood profile. In three of the Brahmyadiyoga-treated patients, elevations of bilirubin, SGOT, and SGPT values were observed.

The results indicate that Brahmyadiyoga had an antipsychotic effect in respect to the symptoms, as evidenced by before and after effect significance. However, the effect was significantly less than that exerted by CPZ. This finding is in partial agreement with the findings of the trial conducted on patients with Unmada (acute schizophrenia). Why Brahmyadiyoga is significantly less effective in the present trial is not clear. It may be due to a difference in potency, a difference in the formulation-using powder of Brahmi instead of juice (as done in the previous study), or because of the need for a higher potency in Anavonmada (chronic schizophrenia) patients.

### **Ayurvedic Treatment Versus Chlorpromazine in Acutely Ill Schizophrenic Patients**

In this rater-blind study,<sup>7</sup> the efficacy of Ayurvedic treatment consisting of both Shodhana (purificatory) and Shamana h the

(palliative) measures was compared with the antipsychotic drug CPZ in acutely ill patients suffering from Unmada (schizophrenia).

Thirty-six patients of either sex in the age range of 16 to 45 years, suffering from Unmada with active psychotic symptoms of a minimum duration of 1 month and less than 10 years were selected. Patients with physical complications or other diseases such as epilepsy or mental retardation were excluded from the study. Eighteen patients each were studied in two treatment groups. Five patients dropped out.

The psychiatric diagnosis was done using the ICD-9.<sup>5</sup> The Ayurvedic diagnosis used the definition and symptoms of Unmada as detailed in the CCRAS Monograph.<sup>8</sup> The psychiatric assessment was done using the Brief Psychiatric Rating Scale (BPRS). The Ayurvedic assessment was done by examining different aspects of Manas (e.g., Buddhi, Smrti, Bhakti, etc.) and the presence or absence of various Lakshana (signs and symptoms) as detailed in the monograph.

The psychological assessment was done using the following tests: reaction time, vigilance, learning, memory function, verbal form, and ideational fluency. Routine blood, urine, body weight, and ECG tests were carried out before and after treatment.

The Ayurvedic treatment consisted of the following:

1. Snehapana with Kalyanaka Ghrita for 3-7 days starting with 15 ml and increasing at the rate of 10 ml per day.
2. Brahmyadiyoga (modified) 500 mg tablets, 2-2-2 and Nidrakarayoga 500 mg capsules, 2-0-2.
3. Mrdu Abhyanga (mild or soft massage) with Dhanwantara Taila for 2 days after Snehapana, followed by Bhashpasweda (steam sudation).
4. Virecana (purgation): oral administration of 75 ml of the Kashaya (decoction) obtained by boiling 10 g each of Aragwadha (*Cassia fistula*), Haritaki (*Terminalia chebula*), and Draksha (*Vitis vinifera*) with 150 ml of water and reducing to 75 ml. Icchabhedi



(1-2 pills) were also administered with the decoction whenever required.

Item 2 was stopped for 2 days on the day of Virecana (purgation) and the next day. If the symptoms did not reduce by 50 percent after 15 days of treatment, the following drugs were added:

5. Kalyanaka Ghrita (10 ml) in the case of Vatapittonmada and Panchagavya Ghrita (5 ml) in the case of Kaphonmada, once a day.
6. Item No. 2 and Unmada Gajakesari Rasa 200 mg plus Sootashekara Rasa 200 mg b.i.d.
7. Saraswatarista 10 ml with Asvagandharista 10 ml b.i.d. after meals.
8. Item No. 3 three times weekly on alternate days.

The CPZ-treated group received the following medications: (1) CPZ 300 mg/day was started as a minimum dosage, which was further increased to 600 mg/day after 15 days if the improvement was less than 50 percent; (2) the anticholinergic drug, Trihexiphenidyl HCl 2 mg was started along with CPZ to reduce the extrapyramidal symptoms.

Diazepam (injection or tablets) was given in unmanageable cases, in both treatment groups. The duration of treatment was 28 days.

When the psychiatric and Ayurvedic assessments were compared with the BPRS, Ayurvedic assessments showed no difference between the two treatment groups in their psychopathological conditions. Within each treatment group, there was a statistically significant reduction in psychopathology in all assessed areas.

The psychological assessment showed significant improvement on some of the statistical tests after the administration of Ayurvedic treatment. The two groups did not significantly differ in the final assessment on any of the tests, indicating that the Ayurvedic treatment could have been as effective as the CPZ treatment. However, significant improve-

ment was seen in the Ayurvedic group in fewer tests than in the CPZ group. Nevertheless, they are indicative of a significant improvement in the cognitive functions of the patient. Thus, the difference in scores (between initial and final) between the two groups did not significantly differ. This confirms the efficacy of the Ayurvedic treatment in bringing about improvement in some of the psychological functions in the patients.

There were no significant before and after differences or between group differences on various laboratory investigations.

In earlier studies, the difference between Brahmyadiyoga and CPZ was not statistically significant, and in a retrospective study,<sup>9</sup> the Ayurvedic general line of treatment was found to be effective in 88.5 percent of the patients with Unmada. The present study suggests that the effects of the Ayurvedic treatment for Unmada are similar to those of the standard antipsychotic drug CPZ.

Another aspect that needs to be looked at is the probability of relapses and occurrences of any long-term adverse effects. Modern drugs are already known to have certain neurotoxic effects, especially movement disorders. If the Ayurvedic drugs are demonstrated to be free from such effects, even with long-term use, that would be a matter of great theoretical interest and practical use.

### **Ksiradhara in Udvega (Anxiety Neurosis)**

Ksiradhara is a special external treatment widely used in diseases of above-the-neck and certain psychological and neurological disorders. In this treatment, certain medicated liquids are streamed over the forehead of the patient.

Udvega (anxiety neurosis) is a very commonly encountered clinical condition. This condition from the Ayurvedic point of view is generally caused by the imbalance of Vata and Pitta Doshas.

Ksiradhara is generally administered for a period of 14 days, starting with 60 minutes on the first day. The duration of the process is increased daily by 10 minutes for the first 7



days and decreased in the same fashion during next 7 days.

In this pilot study,<sup>10</sup> the Ksiradhara a variety of Shirodhara was administered to patients with Udvega (anxiety neurosis). Ten patients of either sex, aged between 20 and 45 years (mean age 24.5) and suffering from uncomplicated Udvega with a duration of 6 months and more and failing to respond to allopathic treatment of at least 3 months duration were selected for the study.

The Ayurvedic diagnosis was done on the basis of signs and symptoms. The modern diagnosis was done by a psychiatrist based on the WHO Glossary of Mental Disorders and Guide to their classification.<sup>11</sup>

The Ayurvedic assessment was based on signs and symptoms present in the patient. Psychiatric and psychological assessments were carried out using Max Hamilton's Anxiety Rating Scale<sup>12</sup> and the Manifest Anxiety Rating Scale<sup>13</sup> by a psychiatrist and a clinical psychologist, respectively.

Ksiradhara was administered for 14 days with 1.5 liters of milk mixed with 2 liters of the decoction obtained by boiling 50 g each of the root-powders of Yastimadhu (*Glycyrrhiza glabra*), Jatamansi (*Nardostachys jatamansi*), and Bala (*Sida cordifolia*) in 6 liters of water.

The Ayurvedic assessment has shown that out of 10 patients, 8 showed significant improvement. The mean improvement of significant level, according to both the Max Hamilton and Tylor Scale are given below:

Scale	Mean	S.E.	E.Value	D.F.	Significance level
Max Hamilton	1.1	2.6	4.166	9	P<0.01
Tylor	7.5	1.9	3.888	9	P<0.02

The improvement in the patients is clearly demonstrated by the statistical test. No side effects were observed. The findings demonstrate the efficacy of this treatment in Udvega (anxiety neurosis), which is resistant to conventional treatment by allopathic medication.

The ingredients of Ksiradharadravya possess qualities which could correct the ng,

vitiation of Vata and Pitta and bring them back to normalcy. In Udvega, Vata and Pitta are imbalanced. Therefore, Ksiradhara may be acting as a Doshapratyaneeka (anti-Doshic) remedy in bestowing relief. Apart from the drug action, the recumbent position enjoyed by the patient during the treatment, the light oil massage given during prolonged streaming, the aroma of the drug, the closure of the eyes of the patient, and the silence observed during the process add to the effect. Ksiradhara is a practical and effective treatment technique for patients with Udvega (anxiety neurosis), even for those who are not responding to conventional psychiatric treatment.

## Conclusion

From the studies conducted, it is clear that the Ayurvedic drugs used in the studies have potentially a positive role to play in the management of psychiatric illnesses. Safety and the absence of side-effects, even with long-term administration, are additional advantages. There is, however, ample scope to augment the drug effects by suitable modifications such as replacement of the whole drug with extracts or altering the recipe for easy administration without affecting the therapeutic efficacy of the drug. These modifications coupled with the inclusion of proper diet and nonphysical measures would certainly make Ayurvedic treatment more scientific and beneficial in the management of psychiatric disorders.

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## Reporter Summary 2

### Symptoms and Diagnosis of Mental Disorders

The session provided an overview of Ayurvedic and allopathic perspectives on the clinical assessment of symptoms and the diagnosis of mental disorders. Dr. Singh presented the Ayurvedic approach and Dr. Issac discussed the Western allopathic approach as delineated in the International Classification of Disease (ICD-10) manual.

In Ayurveda, clinical diagnosis of disease is based on an examination of the strength and vitality or health of the patient (Antara Bala) and the strength of the disease. Antara Bala consists of the nature or quality of the psyche and the genetic makeup of the individual. Dr. Singh presented two fundamental constructs upon which the strength and vitality of the patient are based. The first construct is Prakriti (personality or constitution), which is characterized as a range of normalcy of the quality of the Manas (mind or psyche) and Sarira (physical) Doshas (elements). Prakriti is determined by the genetic constitution of the psyche. Physiological variations in the psyche are predetermined by the interaction of environmental and genetic factors. The second construct is that of Loka Purusa (the macrocosm-microcosm continuum) which states that mental stamina is based on a balance of man and the environment or the universe. The Loka (universe) and the Purusa (individual) are both made up of five basic elements (Pancha Mahabhutas) which are in constant interaction with each other. The main principle of Ayurvedic treatment of a disease is to restore harmony between the Loka and Purusa.

The strength of the disease (Vyadhi Bala) is determined by where it is manifest in the body or in the mind. The diagnosis is based on the Prasna Pariksha (patient interview) and on the Panchendriya Pariksha (physical examination) of the Manas (mental stamina)

of the patient and the state of health of the Sarira (body). The examination serves to assess the balance of the Manasa Doshas (mental elements)-Satva (clarity), Rajas (passion), and Tamas (lethargy)-and the balance of the Sarira Doshas (physical elements) in the Srotas (channels or organs) of the body-Vata (wind), Pitta (bile), and Kapha (phlegm).

The doctor-patient relationship or rapport is very Important in diagnosis and treatment of an individual. The doctor needs to get inside the patient's mind and use his knowledge or insights to describe the etiology, manifestations, and pathology of the disease.

In Ayurveda, it is not necessary to name the disease. Rather, categories of mental illness are described as follows, based on their manifestations and amenability to treatment. Mental illnesses are classified as (1) pure emotional disorders characterized by vitiation of the Doshas of the mind, (2) mixed mental disorders characterized by vitiation of the Doshas of the mind and body such as Unmada (psychosis), (3) psychiatric syndromes which can not be explained by exogenous factors or a role of the Doshas; examples are the Bhutas and Grahas disorders characterized by spirit possession or anger of the gods and given symbolic names of spirits, (4) extreme forms of Prakriti disorders (personality disorders), and (5) other disorders such as mental retardation and senile dementia.

Many different approaches are used to classify diseases in Western or allopathic medicine. The classification of diseases is based primarily on the prominent observable manifestations and the assignment of a name. In general, diagnosis has not progressed to the level of characterization based on morphology or etiology. In some cases, different assessment criteria can lead to variable diagnoses of disease and variable treatment. Dr. Issac cited the United Kingdom/United States study of diagnosis



and treatment of disease as an example of variable international diagnostic criteria between countries with similar cultures resulting in variable treatments for the same disease entity. In the United States, standardized assessments and diagnoses of mental disorders are defined in the DSM-IV, the Diagnostic and Statistical Manual of the American Psychiatric Association.

Dr. Issac stressed the importance of using a standardized, international instrument for assessment and diagnosis of disease in order to be able to compare diagnosis and treatment of diseases within different cultures. Dr. Issac described the ICD-10 (International Classification of Diseases of the World Health Organization) as a standardized, diagnostic instrument that includes lexicons to provide clear definitions of terms. Chapter V of the ICD-10 describes 10 categories of mental and behavioral disorders: three categories dealing with childhood onset of mental disorders such as neurotic, stress, and emotional disorders and seven categories of adult-onset mental disorders such as schizophrenia, mood disorders, organic mental disorders, mental and behavioral disorders due to substance abuse, and others. Chapter V of ICD-10 parallels the DSM-IV. Dr. Issac discussed several assessment instruments such as the CIDI (Composite International Diagnostic Interview) and the Lexica, which provides a clear definition and interpretation of mental health terms.

Dr. Issac stressed the importance of using widely accepted classification and diagnostic criteria detailed in the ICD-10, especially when conducting diagnostic research studies. He indicated that the use of ICD-10 criteria would have great value in its applications to Ayurvedic medicine. He concluded with the statement that standardized diagnoses will be essential in conducting clinical trials of Ayurvedic and allopathic medicines.

### **A Comparison of Ayurvedic and Allopathic Approaches to Patient Interviews**

The session ended with the viewing of a videotape of a patient interview conducted by the Ayurvedic physicians Drs. Ramu and

Singh and a clinical interview of the same patient by the biological psychiatrist Dr. Casper. Dr. Bhatt led a discussion of the Ayurvedic and allopathic approaches to patient interviews. The Ayurvedic interview focused on questions involving the patient's daily routines, habits, and behaviors; the disposition of the mind, the temperament, and emotions before and after onset of the disease; and the physical examination of the pulse, skin, eyes, and so forth. The allopathic interview focused on the signs and symptoms of the disease, the patient's thinking processes, emotions, social conditions, and family history.

Similarities and differences among the two approaches were discussed. The Ayurvedic approach focused mainly on the personality traits of the patient and the imbalance of the Doshas (mental and physical elements), whereas the allopathic approach focused primarily on the signs and symptoms of the disease. The diagnosis of Unmada or psychosis was unanimously agreed upon by Drs. Ramu, Singh, and Casper. However, there were disagreements between the Ayurvedic and allopathic physicians about whether the psychosis was primary or secondary to schizophrenia (primary involvement of Vata Dosha) or to an affective disorder (primary involvement of Pitta Dosha). It was also unclear what role the patient's underlying diabetes played in the precipitation of the Unmada or psychosis. It was agreed that therapeutic testing or response to drug would clearly define the diagnosis and primary Dosha involved in the disorder.

The discussions were very informative, focusing on similarities and differences in the fundamental theories driving the questions used in the Ayurvedic and allopathic approaches to the clinical interview of the patient. The question was asked whether a standardized model can evolve that is acceptable to both Ayurvedic and allopathic approaches to clinical assessment and diagnosis of disease. Dr. Issac suggested that the ICD-10 Chapter V could be a starting place for generating a common clinical assessment and diagnostic instrument. It was agreed that the questions used in clinical diagnoses need to be further refined. The meeting participants agreed that viewing the



patient interview from the Ayurvedic and allopathic perspectives was a valuable experience and a necessary first step in recognizing the need for a standardized, international clinical assessment instrument.

### **Treatment of Mental Disorders**

The session consisted of an overview of Ayurvedic and allopathic approaches to the treatment of mental disorders. Dr. Praveen discussed the use of psychotherapy (Satvavajaya Cikitsa) in Ayurvedic medicine for the treatment of mental disorders and for maintaining good health. Psychotherapy is one of the three streams of therapy used in Ayurveda, the others being rational therapy or diet/ drug therapy (Yuktivyapashraya Cikitsa) and faith therapy (Daivavyapashraya Cikitsa). Psychotherapy is defined as the withdrawal of the mind from harmful objects. Mental illness is due to extreme variations in emotions. Manonigraha (mind control) can be achieved by the use of Yoga. In Yoga, cyclical or measured breathing is one of the ways to fine tune the mind and to control the mind's fluctuations. Dr. Praveen discussed the use of psychotherapy (Yoga) as an essential aspect of good conduct (Swastha Vritta) necessary for mental well-being.

Dr. Casper discussed the use of pharmacotherapy and psychotherapy in the treatment of mental disorders in allopathic medicine. She described the use of these treatments in two main types of mental illness, affective disorder and schizophrenia. In allopathic medicine, psychotherapy is defined as therapy through words and is used primarily as an adjunct to pharmacotherapy. Dr. Casper introduced and discussed the concept of placebo effects as the nonspecific effects of a substance given with therapeutic intent. The therapeutic effects of pharmacotherapy or psychotherapy are assessed by looking at the reduction in symptoms, relapse rates, and recurrence of the disorder and improvements in the level of mental functioning in patients with mental disorders. The healing process consists of (1) self-healing due to the cyclical nature of affective disorders, (2) placebo (nonspecific) influences, and (3) therapeutic interventions (pharmacotherapy and/or psychotherapy). In schizophrenic patients,

pharmacotherapy is the primary form of treatment. Psychotherapy is used in conjunction with pharmacotherapy to promote drug maintenance, decrease relapse rate, ease adaptation of the patient to the social environment, and increase the level of mental functioning of the patient. In affective disorders such as depression, pharmacotherapy and psychotherapy are used together because of their synergistic effects.

Dr. Varier discussed the Ayurvedic approach to treatment of mental disorders as a functional, holistic approach aimed at treating the mind and the body. Ayurvedic medicine focuses on three ways of purifying the mind and body: (1) purification (Samsodhana) consisting of external oleation and internal purification and cleansing therapy by Panchakarma - emesis, purgation, enemas, and nasal instillations; (2) Swastha Vritta, a comprehensive regimen for maintaining health by promoting vigor and good personal conduct according to diet, Yoga, and daily (Dinacarya), evening (Ratricarya), and seasonal rituals (Ritucarya); and (3) curative therapy (Samana) using drugs or Rasayanas (restorative remedies or tonics).

Dr. Mitra led a discussion of Ayurvedic approaches to the treatment of mental disorders. The principles of Ayurvedic medicine are to eliminate the cause of the disease and to purify the mind and body. Panchakarma (internal purification therapy) uses emesis, purgation or evacuation, Ghees (medicated milk), and oleation treatments to cleanse the mind and body; this is the theory of biopurification. Biopurification can be used in conjunction with pharmacotherapy to enhance the efficacy of drug treatments.

The concept of drugs in Ayurvedic medicine includes pharmacological agents and nutrients. Two types of medicines are used in Ayurveda: preventive and curative. Preventive medicines consist primarily of nutrients and are used to promote health and vigor. Purification is typically required prior to the use of preventative medicines. Curative medicines consist of medicinal plants and pharmacological agents and do not typically require the use of purification treatments.

Sound mental health and personal hygiene are important aspects of Ayurveda. Primary



emphasis is put on daily mental and spiritual routines (Dinacarya) and seasonal routines such as when to sleep, eat, and bathe (Ritucarya) rather than on therapies. Dr. Mitra suggested that several bridges can be built between Ayurvedic and allopathic

medicine. One possible bridge is in the use of nutrients or nutraceuticals as health-promoting substances. Another bridge is to focus on the use of pharmacotherapy and psychotherapy as complementary and synergistic treatments for mental disorders.



# Preclinical Studies on CNS Active Agents

C. Nath and G. K. Patnaik

The central nervous system (CNS) is the most complex and important biological system, and it regulates most of the bodily functions, including behavior. Human beings have always been in search of substances which can modify CNS functions, particularly behavior. Ancient Indian medical literature described the use of plants such as *Rauwolfia serpentina* in the treatment of mental disorders. The modern scientific approach for the development of CNS active drugs began in the 1950s, when the potential of psychotropic drugs such as phenothiazines (antipsychotics) and tricyclic antidepressants was realized.<sup>1</sup> The knowledge of dopamine deficiency in Parkinson's disease and its amelioration by administering the dopamine precursor L-DOPA in the early 1960s opened a new era in drug treatment of neurological disorders.<sup>2</sup> Subsequently, neuropharmacological studies on the role of central neurotransmitters in the regulation of behavior and motor, sensory, and autonomic functions in animals as well as in humans laid the basis for the development of novel drugs to treat CNS disorders.

The search for potential new CNS active agents is a continuing exercise for neuroscientists. These drugs can be obtained from natural sources such as terrestrial plants, marine flora, and fauna and by chemical synthesis. CNS active agents can be identified from these sources by using a rational approach based on existing knowledge of a chemical moiety and its structure-activity relationship (SAR); an ethnomedicinal approach based on the traditional use of plants in the treatment of diseases; or by serendipity, namely, incidental discovery without any previous studies.

Any new potential drug acting on the CNS (or other systems) is subjected to extensive experimental testing before it is permitted to be used as a standard drug in the treatment of a disease. The pharmacological evaluation is done in two stages: preclinical testing in

animals and clinical trials in human subjects.

Preclinical studies of CNS active agents is an extensive subject. We have attempted to provide information that is relevant to the basic principles involved in the design and development of the technology to study CNS active agents in animals.

## Basis of Preclinical Testing

Preclinical testing of drugs in animals is based on a common assumption that there is a homology/analogy between the physiology and behavior of various species, such that extrapolation of animal data can be made to humans.<sup>3</sup>

## Objective of Preclinical Studies

The main purpose of preclinical studies is to detect every conceivable pharmacological activity, including the toxicity and the side effects of a drug. A comprehensive study involving a battery of pharmacological tests (*in vivo* and *in vitro*) is carried out to identify and establish the effects and determine the mechanism of action of the drug.

## Basic Factors/Guidelines in Preclinical Studies

In the planning of a preclinical study, it is very important to make proper decisions about the selection of animals, the administration of the drug, and the experimental protocol.

## Selection of Animals

The animals commonly used in CNS studies are albino mice and rats, guinea pigs, dogs, cats, rabbits, and nonhuman primates



(monkeys). The animals are selected according to the objectives of the study. Knowledge about the basic anatomical and physiological features of the animals to be used in the study is always helpful to an experimenter. For example, rodents do not exhibit frank emesis because the vomiting center is absent; dogs are preferred in studies of emesis.<sup>4</sup> Rodents are more docile and easier to handle than cats and monkeys. Some experiments are conducted on birds (pigeons) and fish. Genetically mutant animals are also used.

The maintenance of an appropriate environment for the animals is an essential requirement for the CNS studies, for example, a 12hour light/dark cycle for rats and mice, and organization of a social colony for monkeys.

### **Administration of Drug**

Important factors to consider when administering a drug in animals are solvents to dissolve the drug, doses of drug, and route of administration.

#### **Solvent**

The drug is dissolved preferably in a nonorganic solvent; the best choice is normal saline or distilled water. Organic solvents should be avoided in CNS studies. In case of poor aqueous solubility, the drug can be administered as an aqueous suspension with methyl cellulose or gum acacia.

#### **Dose**

The drug is administered in a nontoxic dose for its pharmacological effects. By convention, the maximal dose should not be more than 10 percent of the LD<sub>50</sub> (lethal dose for 50 percent of the animals) using the same route of administration. The approximate conversion ratio between the doses calculated on the basis of the surface area used for different species is shown in table 1.

#### **Routes**

Drugs are administered either by oral or parenteral routes. The common parenteral routes are intraperitoneal (i.p.), subcutaneous (s.c.), intramuscular (i.m.), and intravenous (i.v.). Certain drugs which do not cross the blood-brain barrier are administered directly

**TABLE 1.** -Equivalent surface area dose conversion factors based on mg/kg doses in one species to mg/kg in another<sup>5</sup>

To:	Mouse 20 g	Rat 150 g	Monkey 3 kg	Dog 8 kg	Man 60 kg
From:					
Mouse	1	1/2	1/4	1/6	1/12
Rat	2	1	1/2	1/4	1/7
Monkey	4	2	1	3/5	1/3
Dog	6	4	5/3	1	1/2
Man	12	7	3	2	1

into the brain by intracerebroventricular (i.c.v.) route, into different brain nuclei by stereotaxic technique, or into the spinal cord by intrathecal (i.t.) route to study the drug's CNS effects.<sup>6</sup>

### **Experimental Protocol**

The design of a preclinical study of a CNS active agent should take the following aspects into consideration.

#### **Grouping of Animals**

The study should include the following groups: an experimental group-treated with the test drug; a control group-treated with the vehicle (solvent for drug); and a standard group-treated with a standard drug which should be active in the treatment condition for which the new drug is being tested. Ideally, the number of animals should be equal in all groups.

#### **Collection of Data**

In behavioral studies, it is always better to get subjective scoring of behavior by a person not aware of the drug treatment in order to eliminate observer bias (blind study). It is not a requisite, however, if the response is being recorded automatically. Time points for observations are decided according to the time course (onset, peak, and duration) of the drug effect.

#### **Statistical Analysis**

Statistical principles are important in grouping, measurement of observations,



analysis of data, and infer-ring a conclusion. There are several statistical tests to determine if observations/measurements made among groups are significantly different.<sup>7</sup> The selection of the appropriate statistical test to analyze the data depends upon the scale of measurement, parametric (interval and ratio interval scale) or nonparametric (ordinal and nominal); and the type of groups (paired or unpaired).<sup>8</sup>

### Preclinical Studies

A preclinical study of a CNS agent includes experiments in primary screening, secondary screening, mechanism of drug action, and toxicity.

#### Primary Screening

The objective of primary screening is to learn about the general activity profile of a drug in normal animals, usually in mice and rats. The effect of a potential CNS active agent is first observed on gross activities of the motor, sensory, and autonomic systems.

#### Motor System

To study the effect of a drug on the motorneuromuscular system, the following parameters are observed: spontaneous locomotor activity, gait, posture, muscle tone, and abnormal signs-stereotypy, catatonia, muscular twitches, tremors, convulsions, Straub tail, and acute neuromuscular deficits.

#### Sensory System

Sensory reflexes tested in primary screening are the pinna, corneal, and righting reflexes. The nociceptive responses of animals to noxious stimuli are also observed.

TABLE2.-Possible major activity of a CNS agent and its therapeutic potential for CNS disorders based on observations of primary screening

Observations	Activity	Therapeutic potential
Hyperkinesia, stereotypy	Dopaminergic	Antiparkinsonian
Hypokinesia, catatonia	Antidopaminergic	Antipsychotic
Increased salivation, lacrimation, urination and defecation, tremors	Cholinergic	Nootropic
Wet dog shakes, lateral head weaving, hind limb abduction, reciprocal treading of forepaws	Serotonergic	Antidepressant
Hypokinesia, loss of righting reflex	Sedative	Antianxiety Hypnotics
Straub's tail	Opioids	Analgesic

#### Autonomic System

The following autonomic responses are observed: salivation, lacrimation, urination, defecation, piloerection, respiration, and body temperature.

Most of the above-mentioned responses are Quantified on a subjective scoring scale. Computerized recording devices are available for some responses, such as locomotor activity, nociceptive reaction, respiration, and body temperature.

The results of primary screening may indicate the possible major activities of a drug (table 2). Primary screening also provides the lead(s) to plan for secondary screening.

#### Secondary Screening

Secondary screening is conducted using animal models which are specific for a particular disease. Responses are used in the animal models to establish and evaluate the efficacy of a drug in comparison with a standard drug. Animal models are experimental preparations that attempt to mimic a human condition or disease by simulating behavioral, neurochemical, or therapeutic aspects of the clinical condition.<sup>3</sup>



aspects of the clinical condition.<sup>3</sup>

### **Evaluation of Animal Models**

Animal models are evaluated for reliability and validity.<sup>3</sup> Reliability indicates consistency and stability of an animal model. It should be evident in consistency in the ability to measure the variable objectives, small variability within and between the subject, reproducibility of phenomenon under similar conditions, and reproducibility of effects of the test drug or procedure.

Validity refers to the usefulness of an animal model for a given purpose. Validity is categorized as follows:

- *Predictive validity.* The capability of a model to identify a property of a drug. For example, activity of a drug which correlates with its therapeutic profile in the clinical situation is termed predictive validity or pharmacological isomorphism. Predictive validity is an important criterion in the selection of animal models for a drug-screening program. Since the predictive validity is assessed on the basis of known effective drugs, it is quite probable that a new drug acting through a mechanism different from the known drug may be missed by even a model of good predictive validity.
- *Construct validity* is related to the accuracy of a measure which is based on the theoretical constructs involved in the genesis of a human disorder.
- *Etiological validity* depends upon the similarities between etiologies in the human condition and the animal model. It is closely related to construct validity.
- *Convergent validity* is the degree to which a model correlates with other models of the same disorder.
- *Discriminant validity* is the degree to which a model measures aspects of phenomena that differ from aspects assessed by other tests. It indicates low correlation between the measures provided by various models.

- *Face validity* refers to the resemblance between the behavioral parameters and responses of an animal model and specific signs and symptoms of the human condition.

### **Animal Models of CNS Disorders**

- Animal models of neuropsychiatric disorders and responses are commonly developed on the basis of the following animal behaviors:<sup>9 10</sup>
- *Elicited behavior.* The behavior specifically induced by a particular drug.
- *Respondent behavior.* The reflexive escape behavior to a noxious stimulus.
- *Operant behavior.* The behavioral (operant) response controlled by consequent events.
- Animal models of the following CNS disorders and responses have been the backbone for preclinical studies on drugs and the diseases.
- Neurological diseases
  - Parkinson's disease
  - Epilepsy
  - Dementia
- Behavioral diseases
  - Psychosis
  - Depression
  - Anxiety
  - Stress
  - Drug/substance dependence
- CNS responses
  - Aggressiveness
  - Nociception
  - Emesis

### **Parkinson's Disease**

Parkinson's disease (PD) is a neurological disorder occurring in elderly persons. The disease is characterized by decreased movements (hypokinesia), muscular rigidity,



resting tremors, and abnormal posture (catatonia). The pathology lies in degeneration of the dopaminergic nigrostriatal tract resulting in an altered balance between the neurotransmitters dopamine and acetylcholine; decreased dopaminergic activity is the primary factor. Dopaminergic drugs are the mainstay of treatment.<sup>11</sup> Other neurotransmitters present in the nigrostriatal system such as GABA, 5-HT, and histamine may also be playing a significant modulatory role in parkinsonism.<sup>12</sup>

### **Animal Models of PD**

A number of animal models have been developed to screen antiparkinsonian agents and to study parkinsonism. Animal models of PD are based on symptomatology and pathology of the disease: decreased dopaminergic activity, increased cholinergic activity, and lesions of the nigrostriatal tract.

#### **Decreased Dopaminergic Activity Model**

Reserpine is known to deplete catecholamine neurotransmitters.<sup>13</sup> Reserpinized rats and mice show hypokinesia, rigidity, catatonia, ptosis, and hypothermia.<sup>14</sup> Of these, hypokinesia, hind limb rigidity, and catatonia are effectively suppressed by antiparkinsonian drugs, particularly by dopaminergic agents. The predictive validity of the hind limb rigidity test is better than tests of hypokinesia and catatonia.<sup>14-15</sup> Dopamine receptor blockade by antagonists such as haloperidol and chlorpromazine also produce similar effects—hypokinesia, rigidity, catatonia—that are not suppressed by dopaminergic drugs. Only anticholinergic drugs are effective against dopamine receptor antagonist-induced effects.<sup>16</sup> Thus, decreased dopamine activity represents a model of drug-induced parkinsonism rather than an idiopathic model.

#### **Increased Cholinergic Activity Model**

Tremorine or its active metabolite oxotremorine, a muscarinic receptor agonist, is used as a tremorogenic agent in rodents.<sup>17</sup> The tremors can be scored on a subjective

scale or be recorded on a chart recorder. Predictive validity is only for anticholinergic drugs.

### **Nigrostriatal Lesion Models**

The nigrostriatal tract (NSD) is destroyed by neurotoxins such as 1-methyl, 4-phenyl tetrahydropyridine (MPTP) or 6-hydroxydopamine (6-OHDA). MPTP is a selective nigrotoxin in human and infrahuman primates. MPTP is formed as a byproduct during the synthesis of a meperidine analog 1-methyl-4-phenyl-4-propionoxypiperidine (MPPP). MPTP is oxidized by monoamine oxidase B into methyl phenyl pyridinium+ (MPP+) which is taken up into dopaminergic neurons and binds with neuromelanin in the substantia nigra.

In primates, MPP+ causes degeneration of nigral neuronal cells, probably by the formation of free radicals which interact with intracellular NADPH (nicotinamide-adenine dinucleotide phosphate, reduced form) cytochrome P450 reductase. However, in rodents, MPTP causes only transient biochemical changes without neuronal degeneration; this may be attributed to the absence of neuromelanin in rodent substantia nigra.<sup>18,19</sup> MPTP produces nonparkinsonian behavioral effects in rodents.<sup>20</sup> In monkeys, multiple doses of MPTP are reported to produce classical parkinsonian effects such as hypokinesia, rigidity, catatonia (hunched posture), and tremors.<sup>21</sup> We have, however, obtained similar effects with a single dose of 2 mg/kg i.m. (unpublished observation). The model has good predictive (dopaminergic and anticholinergic drugs), face, and etiological validity. Prolonging the survival of MPTP-treated monkeys is a problematic task. Some workers have even tried to induce unilateral NST lesions by unilateral infusion of MPTP in the carotid artery.<sup>22</sup>

6-OHDA is taken up into catecholaminergic neurons and is converted into neurotoxic free radicals.<sup>23</sup> Unilateral intrastriatal injection of 6-OHDA in rodents produces retrograde degeneration of the NST, and in these rats, drugs that increase dopamine release (amphetamine, L-dopa) produce circling movements of the animal in the direction of the side of lesion (ipsilateral).



while dopamine agonists (apomorphine, bromocriptine) induce circling in the direction opposite to the lesion (contralateral).<sup>24</sup> The 6-OHDA model is good in predicting dopaminergic activity of an unknown drug and in determining its mechanism of action (i.e., presynaptic or postsynaptic receptor-mediated activity).

## Dementia

Dementia denotes deficits in cognitive functions. The most common is senile dementia of the Alzheimer's type (SDAT), which is characterized by a progressive chronic loss of cognitive functions with severe impairment of recent memory. The characteristic histopathological abnormalities found in brain cortical and hippocampal neurons are neurofibrillary tangles and plaques consisting of deposition of  $\beta$ -amyloid protein. The loss of cholinergic activity in cortical and limbic areas has been implicated in the pathogenesis of SDAT.<sup>11 25</sup>

### Animal Models of SDAT

The following types of animal models produce cognitive deficits which are used as models of SDAT:<sup>25</sup> aged rodents and aged monkeys, anoxic/hypoxic rodents, scopolamine treated animals, aluminum treated animals, excitotoxin lesioned rats or monkeys, and AF64A (cholinergic toxic) lesioned rats.

A drug which improves cognitive functions (learning (acquisition) and memory (retention and recall) assessed by respondent and operant behavior) in these models indicates nootropic or antidementia activity.

Respondent behavior of animals denotes reflex avoidance behavior in response to a noxious stimulus (i.e., escape from the punishment). The avoidance behavior can be active (response) or passive (withholding the response). For example, a rat or mouse avoids the aversive stimulus (electric shock) delivered in one of the arms of a Y maze by not entering that arm (i.e., withholding exploratory response-passive avoidance), whereas in Cook's pole-climbing test, an animal avoids the shocks by emitting a

<sup>10</sup> response (i.e., climbing on a pole-active).<sup>9</sup>

Conditioned respondent behavior involves learning an association between neutral (sound or light) and nociceptive (electric shock) stimuli. A sound is produced prior to or along with an electric shock. After a few trials, animals learn to avoid the shock and escape after exposure to only the sound (Cook's pole-climbing avoidance test).

Operant behavior of an animal is determined by the nature of the event which occurs as a consequence of the operant response of the animal. For example, if a lever-pressing response by a rat is followed by a reward (food), the frequency of the response is increased (positive reinforcement), whereas if a lever-pressing response is followed by punishment (electric shock), the response rate is decreased (negative reinforcement). The consequent event follows either after a specific number of responses (ratio schedule) or after a specific period of time has elapsed (interval schedule).<sup>9 10</sup>

The development of transgenic mice which overexpress the amyloid precursor protein APP-751 messenger RNA was also tried in order to increase the formation of P-amyloid protein in brain, but significant success was not achieved.<sup>26</sup>

## Epilepsy

Epileptic seizures are characterized by the periodic and unpredictable occurrence of transient alterations in behavior due to disordered synchronous and rhythmic firing of a population of neurons (EEG spikes). The amino acid neurotransmitters have been implicated in epileptogenesis. The deficiency of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) or overactivity of the excitatory neurotransmitters glutamate and N-methyl D-aspartate (NMDA) are considered to be the main contributing factors to epileptogenesis.<sup>27</sup> Epileptic seizures are of two types: partial seizures which begin focally in a cortical area with consciousness intact (simple) or impaired (complex); and general seizures which include wide involvement of both cerebral hemispheres from the onset are absence, myoclonic, or tonic-clonic type seizures.<sup>28</sup>



## Animal Models of Epilepsy

There are two types of animal models to evaluate antiepileptic drugs: acute induced seizures (convulsions), the nonepileptic type; and chronic spontaneous seizures, the epileptic type.

### Acute Seizures

Acute seizures are induced by chemicals, electrical shocks, audiogenic stimuli, or photic stimulation.<sup>29</sup>

Chemical convulsants which are used include pentylenetetrazol, picrotoxin, bemegride, bicuculline, strychnine, flurothyl, alumina cream (topical), and cobalt (topical). Among these, pentylenetetrazol is the most commonly used chemoconvulsant. The Seizure Threshold Test uses pentylenetetrazol (85 mg/kg s.c.) to induce clonic seizures in mice, and predicts the effectiveness of drugs in absence (petit mal) seizures. The Maximal Seizure Test uses pentylenetetrazol (38 mg/kg i.v.) to induce tonic-clonic seizures in mice, and assesses the effectiveness of drugs against generalized tonic-clonic (grand mal) seizures.

Electroshock seizures are induced in mice or rats by delivering electroshock through corneal/pinna electrodes. The electroshock seizures are of two types: maximal and minimal electroshock seizures. Maximal electroshock seizures are the tonic type produced by delivery of a 60 Hz, 50 mA current for 0.2 s. It is used to test drugs for grand mal epilepsy. Minimal electroshock seizures are produced by the delivery of 60 Hz, 6-9 mA current for 0.2 s, repeated every 24 h until facial, lower jaw, or forelimb clonus appears without the loss of the upright posture.

Audiogenic seizures can be induced in some inbred strains of rodents that have an increased susceptibility to sound, especially mice and a special breed of rabbit (Beverans). These animals show running and convulsions within 30 s following the sound stimulus. This model is used to test substances against grand mal epilepsy.

Intermittent photic stimulation produces clonus of eyelid and facial musculature and

jaws and violent jerking movements of the entire body in baboons (intermittent light stimulation, 25/s). This model represents photomyoclonic epilepsy and grand mal epilepsy.

### Spontaneous Seizures

Spontaneous seizures, like epilepsy, can be induced by kindling or the administration of pilocarpine.

- *Kindling.* This procedure involves repeated focal stimulation of amygdala or a related brain area by delivery of subconvulsive electrical shocks at widely spaced intervals. Later on, progressively longer and more intense periods of after-discharges are produced at sites both near and distant to the original site of stimulation. Once established, this increased sensitivity persists for the life of the animal. The model reflects a state of longer and more widely propagated seizures with lowered threshold, resembling human epilepsy. The motor seizures vary in degree from running fits to tonus. Hyperactivity of the NMDA receptor and the phenomena of long-term potentiation (LTP) have been suggested as factors which contribute to kindling.<sup>30 31</sup>
- *Pilocarpine.* Repeated administration of pilocarpine induces spontaneous seizures which have been attributed to the loss of inhibitory neurons as a result of pilocarpine-induced overexcitation.<sup>27</sup>

## Schizophrenia

Schizophrenia is an idiopathic psychotic disorder characterized by chronically disordered thinking and emotional withdrawal with delusions and auditory hallucinations. The increased dopaminergic activity in limbic cortex is considered to be the causative factor for schizophrenia. Hyperactivity of dopamine D2 receptors is thought to underlie the positive symptoms of schizophrenia on the basis of therapeutic and neurochemical evidence.<sup>32</sup> Other receptors proposed to be involved in schizophrenia are dopamine D4



receptors for the positive symptoms, dopamine D1 and D3 receptors for the negative symptoms, and serotonin 5-HT<sub>2</sub> receptors.<sup>31 34</sup>

Antipsychotic activity of CNS active agents is studied using animal models of schizophrenia and tests to determine dopamine D<sub>2</sub> receptor antagonism.

### **Animal Models of Schizophrenia**

The animal models are based on neurochemical alterations (dopamine overactivity) and symptoms (hallucination and impaired thinking).<sup>3</sup>

#### **Dopamine Overactivity Model**

Amphetamine, a psychostimulant known to enhance dopaminergic activity and produce psychosis in humans, is used as a pharmacological tool to produce hyperactivity in the dopaminergic system in animals such as rodents and monkeys. In rodents, amphetamine induces a classical hyperactivity syndrome characterized by an increase in locomotor activity, stereotypy, and hyperthermia. The amphetamine hyperactivity in rodents is blocked by antipsychotic drugs.<sup>3</sup> In rhesus monkeys, graded doses of amphetamine (1-4 mg/kg i.m.) produce suppression of approach behavior and contact, body jerking, grooming, hypervigilance (checking), stereotypy, and oral dyskinesia; haloperidol, a dopamine D<sub>2</sub> receptor blocker, inhibits some of the effects.<sup>35</sup>

#### **Hallucinogenic Model**

Since hallucinations are an important feature of schizophrenia, hallucinogenic agents such as lysergic acid diethylamide (LSD) and phencyclidine (PCP) have been tried to develop an animal model of psychosis.<sup>3</sup>

#### **Sensorimotor Gating Model**

One of the possible factors contributing to psychosis is defective sensory gating, a result of sensory overloading which results in cognitive fragmentation. Sensorimotor gating

functions are tested by prepulse inhibition (PPI) of the startle response. Drugs which have been shown to produce sensory gating impairment are amphetamine, PCP, and LSD.<sup>36</sup>

Among all of these models, amphetamine-hyperactivity is considered to be the best on the basis of predictive validity (pharmacological isomorphism).<sup>3</sup>

### **Pharmacological Tests of D<sub>2</sub> Receptor Antagonism**

These tests are an indicator of dopamine D<sub>2</sub> receptors antagonism, which is the most important mechanism thought to underlie antipsychotic activity.

- Antagonism of the behavioral effects induced by D<sub>2</sub> agonists: hyperkinesia, stereotypy, and circling behavior in unilateral 6-OHDA nigral-lesioned rats.
- Catatonia, a sustained abnormal posture, is an outcome of blockade of dopamine D<sub>2</sub> receptors in the corpus striatum and represents an important extrapyramidal side-effect of the antipsychotic drugs, which are D<sub>2</sub> receptor antagonists.<sup>37</sup> Therefore, the development of catatonia indicates the possibility of antipsychotic activity in a drug. Catatonia is tested by the wood block test<sup>38</sup> and the test.<sup>39</sup>
- Conditioned avoidance responses and foot-shock induced aggression. Both of these behavioral responses are inhibited by D<sub>2</sub> antagonists. Anticholinergics and benzodiazepines also suppress these responses.<sup>10 40</sup>

### **Depression**

Depression is an affective (mood) disorder characterized by altered autonomic functions (activity rhythm, sleep and appetite), anhedonia (decreased interest or pleasure in activities), persistent abnormalities in mood, and increased risk of self-harm or suicide.

A lot of work has been done to gain insight into the central neurotransmitter mechani-



sms involved in depression. Hypofunctioning of noradrenergic and serotonergic neurotransmitter systems is regarded as the major neurochemical imbalance underlying depression, on the basis of clinical as well as experimental evidence.<sup>41</sup> The therapeutic activity of an antidepressant drug is attributed to its ability to increase synaptic concentrations of the neurotransmitters and to alter the sensitivity of noradrenergic (beta and alpha) and serotonergic (5-HT<sub>2</sub>) receptors.<sup>42</sup> Experimental studies have also implicated central histamine-2 receptors as facilitators in depression.<sup>43</sup>

### Animal Models of Depression

Animal models of depression are based on depletion of the neurotransmitters norepinephrine (NE) and serotonin (5-HT) and despair-induced behavioral depression. These models of depression have been assessed by Wilner<sup>44</sup> on the basis of validity and grouped as follows:

GROUP 1 (Good): behavioral despair, chronic stress, mother-infant separation in monkeys, and intracranial self-stimulation/reward.

GROUP 2 (Interesting): chronic isolation, yohimbine (dogs), exhaustion stress, and circadian rhythms.

GROUP 3 (Problematic): muricide, olfactory bulbectomy, and learned helplessness.

GROUP 4 (Poor): yohimbine (mice), reserpine reversal, L-DOPA/amphetamine/5-HTP potentiation.

Among these, a few models of depression which are commonly employed to study antidepressant activity of a CNS agent are briefly described.

### Amine Depletion Model

Reserpine is a well known depletor of catecholamines (epinephrine, norepinephrine, and dopamine) and 5-HT and causes depression in humans, even leading to suicide. Reserpine is used to deplete the amine neurotransmitters in animals and produces hypokinesia, rigidity, catatonia,

reversals of hypokinesia, ptosis, and hypothermia are used as predictive measures of antidepressant activity. Pharmacological isomorphism is not very good. Classical tricyclic antidepressants are effective, but atypical antidepressants are not.<sup>45</sup>

### Behavioral Depression Model

- The *swimming despair model of depression* (forced swim test) was described by Porsolt<sup>46</sup> and received wide acceptance. Mice or rats are dropped one at a time in a cylindrical glass jar filled with water up to 9 cm in depth. The animal initially shows vigorous activity to escape from water and then immobility (i.e., floating in the water) interspersed with brief periods of activity. The immobility reflects a state of despair/depression. After the animal is acclimated to the water-filled jar for 2 minutes, the total immobility time during the next 5 min is recorded. The antidepressant drugs, typical as well as atypical, decrease the immobility time. In mice, acute administration of antidepressant drugs is capable of producing antidepressant activity in this model.
- In the *chronic stress model* rats are subjected to an unpredictable variety of stressors including electric shock, immersion in cold water, and reversal of the light-dark cycle for a period of 3 weeks. Then, rats are exposed to loud sound and bright lights followed immediately by the open field test. Exploratory activity is reduced in the stressed rats as compared to unstressed animals. Plasma cortisol levels are also increased in the stressed rats. Daily treatment with antidepressant drugs, typical as well as atypical, is effective in restoration of open field activity and plasma cortisol levels.<sup>3 44</sup>
- *Learned helplessness-induced depression model*: exposure to uncontrollable stress produces a state in rodents similar to human depression (face validity). Typical and atypical antidepressants are effective (pharmacological isomorphism) in this model.<sup>3 44</sup>
- The test of the *intracranial self-stimulation model* is based on the assumption that depression is an outcome of reduced es



Rodents	Human
Loss of appetite	Decreased appetite
Lowered locomotor activity	Psychomotor retardation
Impaired performance in motivated (appetitive and aversive) tasks.	Anhedonia

- reward mechanisms. Lever pressing by rats is coupled with food and electrical stimulation of electrodes implanted in telencephalic/ diencephalic areas (involved in reward mechanisms). After exposure to stress or withdrawal of chronic treatment of psychostimulants, amphetamine or cocaine administration results in a decrease in lever pressing. Antidepressants, typical and atypical, are effective in returning lever-pressing activity to control levels.<sup>3</sup>

### **Anxiety**

Anxiety (neurosis) is characterized by disordered mood changes (anxiety, panic, dysphoria) or behaviors (rituals, hysterical reactions) or minor impairment of thought (obsession).

Underactivity of the GABA-benzodiazepine system is the major contributor to anxiety and, recently, overactivity of the 5-HT system is included as a possible causative factor for anxiety.<sup>47</sup>

### **Animal Models of Anxiety**

Anxiety is induced in animals by punishment procedures, anxiogenic chemicals, and an unfamiliar environment.

### **Punishment Procedures**

Antianxiety drugs improve performance that is reduced by aversive situations. Animal models of anxiety are developed on this basis. Operant or respondent behavior of an animal is suppressed if a noxious stimulus (electric shock) is introduced in the experimental paradigm, probably because of the generation of conflict. An antianxiety agent is capable of restoring the normal

agent is capable of restoring the normal response of the animal in punished operant or respondent behavioral paradigms. A number of experimental paradigms of punished or suppressed behavior are used to test anxiolytic drugs.<sup>10</sup> Some of the commonly used tests are mentioned below.

- *Conflict-neurosis test* (punished operant behavior). Coupling of a positive reinforcer (food) with a noxious stimulus (shock) decreases the response (lever pressing) of the rat. Antianxiety drugs restore the response rate.<sup>48</sup>
- *Voget's test* (punished drinking behavior). Rats receive shocks when making contact with the drinking spout, resulting in a decreased drinking response. Antianxiety drugs reverse the decrease in response rate.<sup>49</sup>
- *Conditioned suppression*. A neutral stimulus (light/ sound) is paired with an unavoidable noxious stimulus (shock) for a brief period in animals responding on an operant schedule for food (positive). During the stimulus period, the responding is suppressed. After several pairings (a process of respondent conditioning), the neutral stimulus itself decreases the responding (lever pressing). This conditioned suppression is also known as conditioned emotional response (CER) and differs from punished behavior in that the aversive stimulus is unavoidable (initially) in the conditioned suppression procedure.<sup>50</sup>

### **Anxiogenic Agents**

The important anxiogenic agents are pentylenetetrazol (metrazol) and p-carboline. Pentylenetetrazol is a convulsant agent which can be used in nonconvulsive doses to induce anxiety in human volunteers and to induce an internal (subjective) state in animals that is equivalent to human anxiety. The anxiogenic effect of pentylenetetrazol is antagonized by a range of antianxiety drugs.<sup>51</sup>  $\beta$ -Carboline, an inverse agonist of the benzodiazepine receptor, also induces an



anxiety- like condition in animals.<sup>52</sup>

## Aggressive Behavior

### Unfamiliar Environment of Animal

Exploratory behavior is inhibited in a novel or strange environment, that is, neophobia. The antianxiety drugs diminish neophobia. There are several tests to study the exploratory behavior of rodents.

- *Maze tests.* The number of entries of an animal into the open and closed arms of a raised 4-arm maze (elevated plus maze) or Y maze is observed. Normally, rodents prefer the closed arms over the open one; this is an indication of fear. The anxiolytic agents increase the number of entries into the open arm(s), implying a reduction in fear-linked anxiety.<sup>53</sup>
- *Staircase test.* The animal is placed in a box containing a five-step staircase. The number of steps climbed (both ascents and descents) and the number of rearing responses (an indicator of anxiety) during a given period are observed. The anxiolytic drugs increase the number of steps climbed and reduce the number of rearing responses.<sup>54</sup>

## Stress

Antistress adaptogens are drugs which induce a state of stress resistance, which is nonspecific, in animals and humans and are capable of countering the maladaptation syndrome.<sup>55</sup> The description of such drugs/substances are available in the ancient literature of Indian medicine, Ayurveda (*Charaka Samhita*). In modern medicine, interest in stress was initiated by Selye, who proposed stress as a biological phenomenon and causative factor for a number of diseases.<sup>56</sup>

A number of tests are required to identify and establish the antistress properties of a drug.<sup>57</sup> Commonly used tests include the swimming endurance test; adrenal functions - weight, ascorbic acid, and cortisol content of the adrenal glands; stress-induced gastric ulcer; hypoxic convulsions; and cold hypoxia restraint stress (CHR).

Aggressiveness is, to some extent, a component of normal behavior. In excess, it is a problem to the individual as well to society. Tranquilizers (antianxiety and antipsychotic drugs) are effective in reducing aggressive behavior. Aggression can be induced in animals (commonly rodents) by several means. Foot shock-induced aggression in rodents is the most widely used model to study the effects of CNS active drugs on aggressive behavior.<sup>58</sup> The central neurotransmitter mechanisms involved in foot shock-induced aggression have been investigated in detail.<sup>40 59 60</sup>

## Drug (Substance) Dependence

Drug (substance) dependence is considered to be a behavioral syndrome which includes a cluster of symptoms resulting from continued use of a drug by an individual despite significant drug-related problems.<sup>61</sup> Compulsive drug intake may be due to the fact that drugs which produce dependence act as positive reinforcers (motivation).

- *Physical dependence* is an altered physiological state because of resetting of the body's homeostatic mechanisms to repeated administration of a drug. Neuroadaptation is the process of counteradaptive changes which occur in the CNS due to the continued presence of a drug; this may lead to development of tolerance and the drug-withdrawal syndrome.
- *Tolerance* is a phenomena in which the effect of a drug is diminished; it is seen during the course of either multiple administration of the same dose (chronic) or after a single treatment with a high dose (acute). When tolerance occurs, a higher dose of the drug is needed to obtain the same magnitude of effect. The administration of a related drug can also induce tolerance (reduce the effect of the other drug); this phenomenon is termed crosstolerance.<sup>62</sup>



- **Withdrawal syndrome.** Termination of drug intake or removal of the drug results in the development of aversive signs and symptoms (psychological and autonomic) which subside when the drug is readministered. The presence of a withdrawal syndrome is considered to be evidence of physical dependence, and its intensity reflects the severity of the physical dependence. The appearance of a withdrawal syndrome is generally attributed to CNS hyperarousal.<sup>62</sup>

### **Animal Models of Drug Dependence**

The animal experiments are designed to test the abuse potential of a drug, tolerance and cross-tolerance, and physical dependence-withdrawal signs.

### **Abuse Potential of a Drug**

The abuse potential of a drug/substance is judged by the drug-seeking behavior of animals (rats and monkeys). Preferential intake of a drug in an experimental setup (self-administration, delivery of a drug through an i.v. catheter by lever pressing) indicates that the drug may act as a positive reinforcer. For example, amphetamine and analogs, cocaine, and opioids are drugs which are liable to engender dependence.<sup>62 63</sup>

### **Tolerance and Cross-Tolerance**

Opioidergic drugs show these phenomena very commonly. For example, with the enkephalin analog (CDRI compound-82/205), we obtained ED<sub>50</sub> values of 5.31, 11.37, and 18.46 mol/kg i.p. in analgesia tests in naive, compound-pretreated and morphine-pretreated mice, respectively.<sup>64</sup> The increase in ED<sub>50</sub> value indicates tolerance to the compound and cross-tolerance to morphine.

### **Physical Dependence**

Physical dependence is evidenced by a withdrawal syndrome following the termination of drug intake or the removal of the drug by an antagonist. For example, when lorazepam administration in rats is stopped

after 23 days (increasing order of dosage schedule), withdrawal signs—hyperkinesia, hyperthermia, hyperaggression, and audiogenic seizures—are seen.<sup>65</sup> Administration of naloxone, an opioid antagonist, in opioid tolerant mice produces a withdrawal syndrome characterized by a jumping response.<sup>66</sup>

## **Animal Testing of CNS Responses**

### **Pain Response (Nociception)**

Pain is the most common unpleasant experience suffered by humans. Therefore, the search for pain-relieving agents has been an unending endeavor for man. The effect of a drug on the pain response can be studied in rats and mice because rodents respond (reflex avoidance) in a predictable manner to a range of controlled painful (noxious) stimuli. The analgesic activity of a drug is assessed quantitatively by the delay in response time of an animal to a painful stimulus. There are several methods to study the effect of a drug on the pain response. The important tests are listed below.<sup>67</sup>

Nociceptive stimulus	Tests	Response
Thermal	Eddy's hot plate (55 -C)	Paw lick and jump
	Heated wire	Tail flick
Tail dip	Warm water (55°C)	Tail flick
	Cold water (-10°C)	Tail flick
	Ethylene glycol	Tail flick
Pressure	Haffner's tail clip	Biting of clip
Inflammation Chemical		Writhing
	Aconitine	Writhing
	Formalin (5 percent)	Licking of paw, flinching, shaking of paw and hindquarters



These animal models represent an acute pain response except for the formalin-inflamed paw test, which indicates continuous (tonic) pain resembling clinical situations of chronic dull pain.<sup>68</sup> Anti-inflammatory analgesics are effective only in the aconitine test. Opioid analgesics are effective on these tests except for the aconitine writhing test. The tail flick response tests are preferred to evaluate kappa opioid analgesics.<sup>67</sup> Morphine-induced analgesia and the straub-tail response are mediated through different subtypes of opioid receptors,  $\mu_1$ , and  $\mu_2$ , respectively.<sup>69</sup>

### Emesis

Emesis is a forceful expulsion of gastrointestinal contents through the mouth and is usually preceded by autonomic signs such as salivation, pallor, sweating, and nausea. Emesis occurs as a common feature in several diseases, as a side-effect of drugs and exposure to ionizing radiation, in pregnancy, travel, and intoxication. Emesis is a reflex process regulated by the vomiting center, which is linked with the emetic chemoreceptor trigger zone (CTZ) located in the area postrema of the medulla oblongata in the brain. The CTZ is located outside of the blood-brain barrier and is very richly innervated by neurotransmitters.<sup>70</sup>

The effects of a drug on emesis is studied in animals, particularly in the dog, which exhibits a frank classical emetic response. The commonly employed emetic agents in dogs are copper sulphate (gastric irritation) and apomorphine (stimulation of dopamine D2-receptors in the CTZ). The ablation of the CTZ helps in determination of the site of action of an antiemetic drug; a centrally acting drug fails to prevent copper sulphate-induced emesis in CTZ ablated dogs. Labyrinthine stimulation (by swinging or cold-caloric test) induced emesis resembles motion sickness and is used to screen antimotion sickness drugs.<sup>4</sup>

### Mechanism of Action

Exploration of the mechanism of action of a CNS active drug is an integral exercise in

preclinical studies. A CNS active drug may produce its effect by acting through a neurotransmitter system or directly on a neuronal membrane. Basic information on the techniques used to study the mechanisms of drug effects on neurotransmitters systems and on neuronal membranes are described below.

### Techniques To Study Neurotransmitter Mechanisms

A drug can modify the turnover (synthesis, release, reuptake, and metabolism) and receptor activity of neurotransmitters.

#### Turnover Studies

*In vivo* and *in vitro* techniques are available to study the turnover of neurotransmitters.

- *In vivo methods.* Microdialysis is used to study the turnover of neurotransmitters, particularly biogenic amines, in conscious, freely moving animals. The microdialysis probe has a semipermeable membrane at the tip; it is placed in the desired brain area, and samples are collected through perfusion at regular intervals. The concentration of amine neurotransmitters (norepinephrine, dopamine, and serotonin) and their metabolites are estimated by HPLC (high pressure liquid chromatography).<sup>71</sup> Voltammetry is another *in vivo* method that measures neurotransmitter levels on the basis of electroactivity of the material in solution.<sup>72</sup>
- *In vitro methods.* Brain homogenates and synaptosomal preparations are commonly used for *in vitro* turnover studies of neurotransmitters. The preparation is incubated with radiolabeled precursor, and depolarizing agents such as K<sup>+</sup> (potassium) or electrical stimulation are used to release the neurotransmitter. Radioactivity in the collected samples is counted to determine the synthesis, release, and reuptake of the neurotransmitter. The activity of synthesizing and metabolizing enzymes are also studied, for example, the enzyme monoamine oxidase (MAO).<sup>73</sup>

#### Receptor Activity

A neurotransmitter acts on a specific



receptor, which is present on the cell membrane, to produce a response. The activity of a drug on a receptor is determined by its affinity and intrinsic activity (response). On the basis of these factors, a drug can act as an agonist, partial agonist, antagonist, or inverse agonist on a receptor as detailed below.

Biochemical characteristics including the genetic sequence of many CNS receptors are known. Receptor activity can be assessed by *in vivo* and *in vitro* techniques.

Affinity	Intrinsic	Benzodiazepine activity	receptor <sup>74</sup>
Agonist	1 (full)	1 (present)	Diazepam
Partial-agonist	1	<1	Abecarnil
Inverse-agonist	1	1 (opposite effects)	$\beta$ -Carboline
Antagonist	1	0 (absent)	Flumazenil

• *In vivo* methods

- *Whole animal studies.* The interactions of specific agonists and antagonists of neurotransmitters are studied on the significant effect of the drug, using behavioral and physiological responses in animal models described earlier. For example, the analgesic activity of the CDRI compound 82/205 is blocked by pretreatment with the specific mu opioid receptor antagonists,  $\beta$ -FNA (funal-trexamine) and naloxonazine ( $\mu$ l), indicating that the compound is a  $\mu$ -receptor agonist.<sup>64</sup>

- *Isolated tissue preparations.* The responses of different tissues are mediated by specific receptors for a particular neurotransmitter. Some of the commonly used tissue preparations and their receptor specificity are given below.<sup>75</sup>

Tissue preparation	Receptor type
Guinea pig ileum	Opioid, $\mu$
Mouse vas deferens	Opioid, $\delta$
Rabbit ileum	Cholinergic, muscarinic
Rat uterus	Serotonergic

The effect of drug on the response of a given tissue preparation and its interaction with specific agonists or antagonists indicates the receptor activity of the drug.

• *In vitro* methods. *In vivo* studies of receptors, ranging from their anatomical location to their genetic expression, have tremendously improved our understanding of receptor function at the cellular and molecular levels. A brief description of *in vitro* techniques commonly employed to study the effects of drugs on receptors are provided here.

- *Radioligand receptor binding assays.* The radioligand binding assay is probably the most widely used *in vitro* method in neuropharmacological research. The assay determines the affinity of a drug for a receptor, one of the most important determinants of its actions. The assay is designed on the basis of competition between a radiolabeled *ligand* (agonist or antagonist) and unlabeled drug to bind to a particular receptor.

The radioligand binding receptor assay is based upon the principle law of mass action.<sup>76</sup>



where  $[R_f]$  is the concentration of free receptor,  $[D_f]$  is the concentration of free radiolabeled ligand, and  $[RD]$  is the concentration of ligand-bound receptor.

The total concentration of ligand,  
 $[D_t] = [D_f] + [RD]$ .

The total concentration of receptor,  
 $[R_t] = [R_f] + [RD] - B_{max}$ .

The dissociation constant,  
 $K_d = [R_f] [D_f] / [RD]$ .

The affinity of a ligand/drug for a receptor is indicated by the  $K_d$  value, and the number of receptors is indicated by  $B_{max}$ . Additional information about the affinity of a drug for a receptor is obtained by the  $IC_{50}$  value, that is, the concentration of drug (unlabeled) which decreases the binding of the radioligand by 50 percent.



There are several ways to analyze the radioligand receptor assay, for example, Scatchard analysis and Hill plot. Important factors which can influence receptor binding are stability of the receptor and radioligand, the concentration of the radioligand (at or below the  $K_d$ ), nonspecific binding, and multiple binding sites. Radioligand binding assays are accurate and rapid tests (requiring a very little amount of the drug) to determine the receptor activity of a drug. However, conclusions should be drawn only after correlating the data with *in vivo* experiments.<sup>76 77</sup>

**Molecular pharmacology of receptors.** Stimulation of a G-protein coupled neuroreceptor induces the formation of specific G-proteins (GTP-binding protein complex) which regulate the cascade of intracellular enzymatic activities (enzyme effector systems) such as adenyl cyclase, protein kinases, phosphatases, inositol phosphates, diacylglycerol, phospholipase, and even ion channels.<sup>78</sup> Studies on the effects of a drug on these biochemical consequences of receptor activity (second messenger systems) shed light on the molecular mechanisms of the drug.

**Molecular genetics of receptors.** The techniques of molecular genetics have unveiled the face of the receptor to pharmacologists to whom the receptor was an "unknown beautiful lady" for a long

time. The formation of receptors is genetically coded, and the receptors of many neurotransmitters have been cloned. The techniques used to clone a receptor are very complicated and tedious. The major steps involved in cloning of a receptor, present in the brain, are outlined below in a simplified manner.<sup>79</sup>

cDNAs of the receptor are introduced into test cells (frog oocytes and mammalian cells) for expression of the receptor protein so that the receptor activity can be assessed by specific receptor ligand assays and second messenger functions.

### Techniques To Study Neuronal Membrane Mechanisms

The function of the CNS depends upon the integration and propagation of electrical events in neuronal cells. A drug can modify neuronal electrophysiology by either receptor stimulation or by altering ionic conductance directly.

The important electrophysiological techniques used to study the effects of a CNS active drug on neuronal activity are microiontophoresis, electroencephalogram (EEG), and patch clamp or voltage clamp.

Microiontophoresis records the effect of highly localized drug administration on the electrophysiological activity of a single neuronal cell. EEG determines the effect of the drug on the overall electrical activity of the brain. The clamp techniques, patch or voltage, are used to study the electrical properties of a single ion channel and the regulation of the channels by drugs or neurotransmitters. For *in vitro* electrophysiological studies of neuronal cells, acutely isolated neurons from brain slices, chronically cultured neurons, or brain slice cultures are used.<sup>80</sup>

### Toxicity Studies

It is an essential part of any preclinical study to determine the toxicity of a drug. The drug is subjected to general and specific toxicity tests.

### General Toxicity

The drug is studied for acute (24 hours) and

#### Steps for Receptor Cloning

1. Purified mixture of brain mRNAs  
↓ Reverse transcriptase
2. Single stranded complimentary DNA (cDNA)  
↓ Self-template
3. Double-stranded complimentary DNA  
↓ Insertion into bacterial plasmid
4. Recombinant complimentary DNA plasmid  
↓ Insertion into engineered bacteria and replication
5. Brain complimentary DNA library  
↓ Isolation and purification of a particular receptor by selective binding assays
6. Pure complimentary DNA (cDNA)-cloned receptor



chronic toxicity (administration for 3 weeks to 2 years depending upon the intended period of use in humans). The regulatory toxicity is preferred in two species and by two routes (parenteral, 3 days mortality, and oral, 7 days mortality). The subacute or chronic toxicity study is done on two species, one rodent and one nonrodent. During the study, gross behavior, food intake, and body weight are recorded regularly. Biochemical estimations in blood and urine are done periodically. Histopathological examinations of vital organs are also performed.

### **Specific Toxicity**

Specific toxicity tests are employed to study the effects of the drug on the fetus (teratogenesis), genes, and development of malignancy (carcinogenesis).

Teratogenic studies are conducted in three phases.<sup>81</sup> Phase I includes the study of gonadal effects of the drugs in males and females-ovarian cycle, mating, conception rates, late gestation, parturition, and overall effects. Phase II is done in two species. The fetuses are examined for gross malformations, preimplantation death, resorption, live and dead births, and body weight of live births. In Phase III, perinatal and postnatal effects of the drug are observed.

Mutagenesis should be studied in two to three generations. Development of malignancy should be observed for at least one lifespan.

### **Recent Advances**

Future research in neuropharmacology will benefit from the application of recently developed molecular genetics techniques. These techniques are mainly targeted by genetic manipulations of receptor activity. The techniques include antisense oligodeoxynucleotides and transgenic animals.

#### **Antisense Oligodeoxynucleotides**

Antisense oligodeoxynucleotides (AS) to receptor mRNA can be taken up by receptor-mediated endocytosis. AS blocks the ability of receptor (cDNA) to form protein, so that a particular receptor is inactivated.<sup>82</sup> The use of

AS is very helpful in studies of receptor systems in which a specific antagonist is not yet available. For example, repeated i.c.v. administration of AS to the neuropeptide Y1 receptor mRNA in rats reduced Y1 receptor levels 60 percent without affecting Y2 receptors and produced anxiogenic behavior which was reversed by anti-anxiety drugs.<sup>83</sup> AS to dopamine D2 receptor mRNA produces a decrease in D2 receptor levels, D2 receptor mRNA levels, and circling behavior in nigral lesioned rats, indicating a specific inactivation of D2 receptors.<sup>84</sup>

### **Transgenic Animals**

Animals can be developed with a specific mutation (overexpression or deletion) in any cloned gene. The method involves introduction of a desired gene mutation into the embryo by retroviral infection, manipulation of embryonic stem cells, or direct micro-injection into the fertilized egg, eventually leading to the development of a line of mutant animals. The injection of purified mRNA for normal rat hypothalamus or synthetic copies of vasopressin mRNA into Brattleboro rats (animals which lack the gene for hypothalamic vasopressin) produced vasopressin expression for several days.<sup>84</sup>

"Knock out" animals are those in which a particular gene responsible for encoding a receptor or enzyme is inactivated. Animals with a mutation in the gene encoding alpha-Ca<sup>2+</sup> calmodulin dependent kinase II (CAM kinase II) synaptic protein, which is present in high amount in the hippocampus in wildtype animals, exhibit impaired cognitive functions and long-term potentiation (LTP). The behavioral profile of the CAM kinase II knock out animals is similar to that of wildtype (normal) animals with a hippocampal lesion.<sup>85</sup>

### **Conclusion**

Preclinical studies are critical to drug development. The maximum possible information about a drug can be obtained by designing experimental protocols in animals which are not possible in humans. Several animal models are available to study and



predict the effects of novel drugs in human CNS disorders. Hopefully, more animal models will be developed in the future due to advances in our understanding of CNS diseases and in the development of molecular biological technologies.

Different experimental models and tests provide significant information related to different aspects of a particular CNS disorder. Therefore, experimental models and tests should be selected according to the objectives of study. For drug screening, the predictive validity (pharmacological isomorphism) is the major criterion in selection of the animal model. It is desirable to correlate results of *in vitro* tests with the effects of a drug on the integrated response of an animal.

Extrapolation of data from animals to humans requires careful interpretation of experimental observations. In spite of some doubts and questions about the relationship between clinical disease and its experimental model in animals, animal models of disease have led to dramatic advances in the development of new drugs and in our understanding of human diseases.

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# Contemporary Animal Models for Testing Pharmacological Impact

M. A. Geyer, A. Markou and N. R. Swerdlow

This chapter first examines the process of developing and validating animal models relevant to psychiatric disorders and then illustrates this process using a particular model of the sensorimotor gating deficits observed in patients suffering from disorders of schizophrenia or, in Ayurvedic terms, unmada. In general, a model is defined as any experimental preparation developed in order to study a particular condition or phenomenon in the same or different species. In the present context, models are typically animal preparations that are used to mimic some form of psychopathology in humans.

In developing and assessing an animal model, one must first consider the purpose intended for the model, because the intended purpose determines the criteria that the model must satisfy to establish its validity. At one extreme, one can attempt to develop an animal model that mimics a psychiatric syndrome in its entirety. In the early years of psychopharmacology, the term "animal model" often denoted such an attempt to reproduce a psychiatric disorder in a laboratory animal. Unfortunately, this approach is fraught with difficulty because it typically relies upon arguments of apparent similarities (i.e., face validity) that are difficult to defend and because the symptoms characterizing psychiatric disorders are often defined in subjective terms. Indeed, both intranational and international efforts to establish agreement in the definitions of psychiatric disorders have had a complex history and met with only limited success. It is not uncommon for diagnostic categories to be split into multiple new entities or combined into a new category as clinical experience reveals the limitations of previous categorizations. Given that the diagnostic categories themselves are continuously being revised and redefined even within one tradition, it should not be surprising that we have some difficulties in our attempts to find common ground between the Ayurvedic and

allopathic traditions.

A more limited use of an animal model is to focus only on the effects of potential therapeutic treatments. In such a case, the model may or may not mimic the actual psychiatric disorder. Rather, the model is intended only to reflect the efficacy of known therapeutic agents and thus lead to the discovery of new pharmacotherapies. Because the explicit purpose of the model is to predict treatment efficacy, the principle guiding this approach has been termed "pharmacological isomorphism."<sup>1</sup> The fact that such models are developed and validated by reference to the effects of known therapeutic drugs, however, frequently limits their ability to identify new drugs having different chemical structures or novel mechanisms of action. An inherent limitation of this approach is that it is not designed to identify new therapeutics that might treat the symptoms of the disorder that are refractory to current treatments.

Rather than attempt to mimic an entire syndrome, a more reductionistic approach to the development of animal models focuses only on specific signs or symptoms associated with psychopathologic conditions. In such cases, specific observables that have been identified in psychiatric populations provide a focus for study in experimental animals. The particular behavior being studied may or may not be pathognomonic for or even a defining symptom of the disorder, but must be defined objectively and observed reliably. Thus, even phenomena that are found in more than one diagnostic entity may be studied in animals using this approach. The reliance of such a model on specific observables minimizes a fundamental problem plaguing animal models of psychopathology designed to model diagnostic syndromes. Specifically, the number of definitive clinical findings with which one can validate an animal model have been limited by the difficulties inherent in conducting experimental studies of psychia-



tric populations. The validation of any animal model can be only as sound as the information available in the relevant clinical literature<sup>2</sup> With this approach, the investigator may generate more definitive information related to a more circumscribed domain of psychopathology. By limiting the purpose of the animal model, one can increase the confidence in the cross-species validity of the model. The narrow focus of this approach generally leads to pragmatic advantages in the conduct of mechanistic studies addressing the neurobiological substrates of the behavior in question. By contrast, in models intended to reproduce entire syndromes, the need for multiple simultaneous endpoints makes it relatively difficult to apply the invasive experimental manipulations required to identify underlying mechanisms.

Another approach to the development of animal models is more theoretically based upon psychological constructs that are thought to be affected by the psychiatric disorder under investigation. Such an identification of what has been termed psychological processes or behavioral dimensions<sup>1 2</sup> involves the definition of a hypothetical construct and subsequent establishment of operational definitions suitable for the experimental testing of the validity of the construct.

This approach is most fruitful when conceptually related experiments are undertaken in both the relevant patient population and in the putative animal model. First, studies of appropriate patients are needed to establish the operational definitions of the hypothetical construct and the construct's relevance to the particular disorder. In concert, parallel studies of the theoretically homologous construct, process, or dimension are required to determine the similarity of the animal model to the human phenomena. An important advantage of this approach is that the validation of the hypothetical construct and its cross-species homology can be established by studies of normal humans and animals, in addition to psychiatrically disordered patients or experimentally manipulated animals. Thus, this approach benefits from the psychological and neuroscientific literature relevant to the

hypothetical construct upon which the model is based. In a sense, this approach explicitly recognizes that the experimental study of the disorder in humans involves as much of a modeling process as does the study of the disorder in an animal model.

### **Criteria for Evaluating Animal Models**

Validation criteria are standards that are relevant to the evaluation of any model and have been discussed in several relevant reviews.<sup>1-6</sup> In general, the validity of a model refers to the extent to which a model is useful for a given purpose. In neurobiological research, the typical purpose of a model is to promote our understanding of a human condition that is expressed behaviorally by elucidating the neurobiological mechanisms underlying the human condition. Here it will be argued that there are only two criteria that a model must satisfy to establish its value in basic neurobiological research: reliability and predictive validity.<sup>3</sup> While the satisfaction of other criteria, such as construct validity, may have heuristic value, it is not essential.

#### **Reliability**

Reliability refers to the consistency and stability with which the variable of interest is observed. This consistency should be evident at several levels: (a) ability to measure the variable objectively, (b) small within-subject variability, (c) small between-subject variability, (d) reproducibility of the phenomenon, and (e) reproducibility of the effects of manipulations.<sup>5</sup> Having a reliable and reproducible experimental system is essential to scientific study.

#### **Predictive Validity**

Predictive validity is generally defined as the ability of a test to predict a criterion that is of interest to the investigator.<sup>7</sup> For animal models, the criterion is the human phenomenon. An animal model has predictive validity to the extent that it allows one to make predictions about the human phenomenon based on the performance of the model. Thus, development of animal models



requires parallel development of clinical measures that will allow meaningful comparisons. For animal models of human psychopathology, the term predictive validity is often used in a narrow sense to refer to the model's ability to identify drugs with potential therapeutic value in humans (i.e., pharmacological isomorphism<sup>18</sup>). Although correct, this use of the term is limited because it ignores other important ways in which a model can lead to successful predictions.<sup>2</sup> For example, the identification of any variables that influence both the experimental preparation and the modeled phenomenon in similar ways or correlations with other measures can help in assessing the predictive validity of a model.

### **Construct Validity**

Construct validity of a test refers to the accuracy with which the test measures what it is intended to measure.<sup>7</sup> Although construct validity is considered by some investigators as the most important property of a test,<sup>7, 8</sup> it can be established only rarely. The process of construct validation of a test is not different in any essential way from the general scientific procedure for developing and testing theories and thus for developing animal models. Conceptions about what a model is supposed to mimic are constantly changing as scientific theories and theoretical constructs are modified. Thus, a model's usefulness, and hence its overall validity, cannot be determined by the degree of construct validation that it has. Nevertheless, the process of construct validation is valuable in the ongoing process of further development and refinement of the model. As new experimental and observational evidence accrues from both the animal model and the clinical conditions, the model is refined and therefore enables more accurate predictions.

### **Etiological Validity**

The concept of etiological validity is closely related to the concept of construct validity. A model has etiological validity if the etiologies of the phenomenon in the animal model and the human condition are identical. When

etiological validity can be established, the model can become extremely useful in the development of treatments. The limitations of treatment-oriented models based on pharmacological isomorphism can be overcome if an etilogically based model is found. Unfortunately, the etiologies of psychiatric disorders are seldom known. Hence, etiological validity in this context is generally limited to speculations or hypotheses regarding a possible etiology. Indeed, the purpose for the development of animal models is often to enable the identification of the etiology of the disease. Like construct validation, the process of etiological validation is a fundamental component of scientific investigation.

### **Face Validity**

Face validity refers to the phenomenological similarity between the behavior exhibited by the animal model and the symptoms of the human conditions. Although face validity appears to be a desirable criterion with which to validate models,<sup>10, 11, 12</sup> such a criterion is actually not necessary, can be misleading, and is difficult to defend rigorously. While the majority of models involve cross-species comparisons, it is unrealistic to expect different species to exhibit similar symptoms or phenomenology, even in cases where the etiology of the condition is known.<sup>1, 2</sup> Indeed, finding similarities between certain aspects of the behavior or physiology of animal and humans does not necessarily indicate similar etiology.<sup>4, 13</sup> Moreover, objectively establishing the face validity of a model is virtually impossible. Although face validity can provide a heuristic starting point for the development of an animal model, it cannot be used to establish the validity of the model. Claims for face validity almost invariably involve subjective arguments that are not amenable to proof. It should be understood that face validity refers to the superficial similarity in symptomatology between the model and the disorder and can be distinguished from construct validity, which relies on similarities in underlying processes. Thus, while face validity does not detract from an animal model, it simply does not provide scientific support for a model.



## **Modeling Sensorimotor Gating Deficits in Schizophrenia**

The remainder of this chapter illustrates the development and use of a particular animal model of relevance to the varieties of schizophrenic psychoses, or, in Ayurvedic terms, *unmada*. The particular model is focused on a hypothetical construct of deficient gating or filtering mechanisms as a set of potential etiologic factors that could produce a range of behavioral syndromes having some common signs and symptoms. The model does not depend upon a particular diagnostic formulation of a singular disease entity and is therefore compatible with the idea that the broad category of schizophrenia or *unmada* includes a variety of disorders. Rather, the work to be described begins with a reductionist approach to the identification of an objectively defined operational measure of sensorimotor gating that can be studied using homologous behaviors in rodents and humans. A particular advantage of this approach is that such objective measures should facilitate experimental studies of the efficacy of either allopathic or Ayurvedic treatments while minimizing the need for predetermined agreement on diagnostic classifications of disease.

Clinical observations in schizophrenia-spectrum patients have identified deficiencies in the processing of information, including inability to automatically filter or "gate" irrelevant thoughts and sensory stimuli from intruding into conscious awareness. Accordingly, theories describing the group of schizophrenias often conceptualize the common aspect of these disorders as involving one or more deficits in the multiple mechanisms that enable normal individuals to filter or gate most of the sensory stimuli they receive.<sup>14-16</sup> Collectively, this class of mechanisms is referred to as sensorimotor gating. Theoretically, impairments in gating lead to sensory overload and cognitive fragmentation.

The hypothetical construct of sensorimotor gating has been operationalized and explored in both human and animal studies. Among the approaches our group has taken to developing operational measures of this theoretical construct, the most productive has

taken advantage of the opportunity to study homologous forms of behavior using the startle response. For example, numerous studies have examined startle habituation deficits in schizophrenic patients,<sup>17-18</sup> which may reflect failures of sensory filtering that could lead to disorders of cognition. As discussed below, the validity of this gating construct has been assessed most thoroughly using another operational measure based on the homologous nature of the startle reflex, namely the prepulse inhibition (PPI) of startle paradigm.

The startle reflex is a constellation of responses to sudden intense stimuli that has long been studied as a way to understand the neural control of simple behaviors. One major advantage of startle response paradigms is that homologous behavioral phenomena can be studied in a variety of species. In humans, the blink reflex component of the startle response is measured using electromyography of the orbicularis oculi muscle. In rodents or guinea pigs, a stabilimeter chamber is used to measure the whole-body flinch elicited by stimuli that are identical to those used in humans.

Of importance for the present work is not the reflex phenomenon itself, but the conceptually important forms of behavioral plasticity that are regulated by forebrain circuitry and can be demonstrated using measures of startle. One form of startle plasticity is PPI, which is the normal suppression of the startle reflex when the intense startling stimulus is preceded by a weak prestimulus.<sup>19-21</sup> In PPI, a weak prepulse inhibits a reflex response to a powerful sensory stimulus. Prepulse inhibition occurs when the prepulse and startling stimuli are in the same or different sensory modalities.

Apparently, all mammals, including primates, exhibit PPI. It does not appear to be a form of conditioning, since it occurs on the first exposure to the prepulse and pulse stimuli, and it does not exhibit habituation or extinction over multiple trials. PPI thus appears to reflect the activation of ubiquitous "hardwired" centrally mediated behavioral gating processes that are regulated by forebrain neural circuitry. Virtually all the evidence available supports the belief that PPI



is homologous from rodents to humans.

Our first report of deficits in PPI of acoustic startle in schizophrenic patients appeared in 1978.<sup>22</sup> Since that time, our laboratory and others have confirmed this finding in schizophrenia<sup>23-26</sup> and have extended it to the identification of PPI deficits in obsessive compulsive disorder,<sup>27</sup> Huntington's disease,<sup>28</sup> nocturnal enuresis and attention deficit disorder,<sup>29</sup> and Tourette's syndrome.<sup>30</sup> These disorders are all characterized by a loss of gating in sensory, motor, or cognitive domains and by abnormalities in cortico-striato-pallido-pontine circuitry that modulates ppl.<sup>31</sup> Importantly, PPI deficits are not unique to a single form of psychopathology. Instead, these deficits are the result of abnormalities within a specific, defined brain circuit. Deficits in PPI in schizophrenia patients do not simply result from gross behavioral impairment or medications, since schizotypal patients who are not grossly psychotic or receiving antipsychotic medications also show PPI deficits.<sup>32</sup>

## Pharmacology of Prepulse Inhibition in Animals

### Dopamine

Dysfunction in dopamine (DA) systems has long been implicated in the pathophysiology of schizophrenia. In rats, PPI is reduced by drugs that facilitate DA activity, including the direct DA agonist apomorphine<sup>33-39</sup> and the indirect DA agonists d-amphetamine<sup>34</sup> and cocaine, and these effects are reversed by DA receptor antagonists.<sup>34 36-39</sup> As in patients with schizophrenia,<sup>24</sup> the apomorphine-induced disruption of PPI is not modality specific, being seen when acoustic prepulses are used to inhibit either acoustic or tactile startle.<sup>40</sup> The D<sub>2</sub> receptor appears to mediate the apomorphine-induced disruption of PPI, since this effect of apomorphine is blocked by the D<sub>2</sub> antagonists haloperidol, raclopride, and spiperone.<sup>34 37</sup> Further support for a role of the D<sub>2</sub> receptor, but not the D<sub>1</sub> receptor as a primary substrate of PPI is the finding that PPI is disrupted by the D<sub>2</sub> agonist quinpirole, but not by the D<sub>1</sub> agonist SKF 38393.<sup>41-43</sup> While evidence from our laboratory<sup>41 43</sup> and others<sup>33</sup> indicates that D<sub>1</sub> and D<sub>2</sub> receptors may interact in the regulation of PPI, D<sub>1</sub>

receptors do not appear to serve as an independent substrate for changes in PPI. The apomorphine-induced disruption of PPI is reversed by the atypical antipsychotic clozapine,<sup>37 39</sup> which lacks neuroleptic properties in some behavioral assays, and the putative atypical antipsychotic seroquel.<sup>31</sup> Recently, it was reported that the putative D<sub>4</sub> antagonist NGD 94-1 restores PPI in apomorphine-treated rats, despite the fact that it is inactive in traditional preclinical measures of antipsychotic action.<sup>44</sup> Thus, there is converging evidence for the important involvement of dopaminergic systems, acting via D<sub>2</sub>-family receptors, in the control of PPI. These findings in rats parallel the deficits in PPI observed in schizophrenia patients,<sup>22 24</sup> which are also reported to be corrected by both typical and atypical antipsychotics.<sup>26 45</sup>

Several studies suggest that the effects of DA agonists on PPI are mediated by increased DA activity in the NAC. First, low doses of apomorphine that do not decrease PPI in control rats potently disrupt PPI in rats that are surgically altered to have "supersensitive" DA receptors in the NAC.<sup>46</sup> Second, the loss of PPI induced by the indirect DA agonist amphetamine is reversed by depletion of DA in the NAC.<sup>47</sup> Third, PPI is disrupted in rats by infusion of the D<sub>2</sub> agonist quinpirole or DA into the NAC or anteromedial striatum (but not the orbital cortex, amygdala, or posterior striatum).<sup>48 49</sup> The effects of intra-NAC quinpirole or DA infusion on PPI are reversed by systemic treatment with D<sub>2</sub> antagonists.<sup>42 43</sup> Fourth, *in vivo* microdialysis studies of DA levels in the NAC during startle testing have demonstrated that startling stimuli produce a decrease in dialysate DA in the NAC and that this decrease is blocked by prepulse stimuli.<sup>50</sup> Thus, overactivity of NAC DA may be a substrate for the loss of PPI produced by systemic administrations of DA agonists in rats.

Most predictive models for antipsychotic agents, such as the reversal of apomorphine-induced canine emesis<sup>51 52</sup> and rodent stereotypy,<sup>51</sup> assess the ability of a compound to reverse a physiological (behavioral) effect of a DA agonist. Many DA receptor antagonists identified in this manner are clinically useful "typical" antipsychotics that are highly effect-



ive in reducing hallucinations and delusions—the "positive" symptoms of schizophrenia. In contrast, "negative" or "deficit" psychotic symptoms— affective flattening, alogia,

or avolition—are linked theoretically to reduced forebrain glutamate transmission.<sup>53</sup> Some evidence indicates that these deficit symptoms respond to atypical, but not typical antipsychotics.<sup>55</sup> These atypical antipsychotics, like clozapine, are also associated with a much lower risk for acute parkinsonian sideeffects; to date, no evidence firmly links the use of clozapine alone to the development of tardive dyskinesia, a common and severe side effect of typical antipsychotic agents. Unlike the multiplicity of animal models capable of predicting the antidopaminergic properties of "typical" antipsychotics, no animal model has convincingly demonstrated such predictive validity for identifying agents with atypical antipsychotic properties. For example, clozapine fails to reverse amphetamine- and apomorphine-induced stereotypy in rats or apomorphine-induced emesis in dogs.<sup>51</sup>

The ability of antipsychotics—including the "prototypic" atypical antipsychotic clozapine to restore PPI in apomorphine-treated rats strongly correlates with their clinical potency ( $R=0.99$ ).<sup>31 38 39</sup> In addition to its sensitivity, the specificity of the PPI model for compounds with antipsychotic efficacy is supported by reports that it predicts no such efficacy for buspirone, diazepam, imipramine, naloxone, or propranolol.<sup>56</sup> Thus, the PPI paradigm appears to be sensitive to both typical and atypical antipsychotics, but when used with the DA agonist apomorphine, this paradigm clearly fails to make the potentially important distinction between these two classes of antipsychotic agents.

### Glutamate

In addition to its disruption by DA agonists, PPI is also reduced or eliminated in rats by psychotomimetic noncompetitive glutamate (NMDA) antagonists, such as phencyclidine (PCP), dizocilpine (MK-801), and ketamine.<sup>57 58</sup> As with apomorphine or schizophrenia, both intramodal and cross-

NMDA antagonists.<sup>40</sup> In contrast to the effects of DA agonists on PPI, those of NMDA antagonists are not reversed by typical antipsychotics such as haloperidol<sup>40 59 60</sup> or selective D<sub>1</sub> or D<sub>2</sub> antagonists,<sup>61</sup> but are reversed by the atypical antipsychotics clozapine,<sup>61</sup> olanzapine,<sup>62</sup> seroquel,<sup>60</sup> and remoxipride.<sup>63</sup> These findings raise the possibility that the PCP-disruption of PPI might be a useful model for identifying compounds with atypical antipsychotic potential. Such predictive validity might be accompanied by construct validity, since PCP-induced clinical and glutamatergic neurochemical effects have been linked to the characteristics and pathophysiology of "deficit" symptom schizophrenia. In humans, this class of drugs produces symptoms that mimic some features of schizophrenia.<sup>54</sup> Furthermore, ketamine has been shown to reduce PPI in normal control subjects,<sup>64</sup> providing some validation of the similar animal studies.

### Serotonin

Prepulse inhibition in rats is reduced by systemic treatment with 5-HT releasers, including 3,4-methylenedioxy-N-methylamphetamine (MDMA), N-ethyl-3,4-methylenedioxy-amphetamine (MDEA), fenfluramine, and alpha-ethyltryptamine (AET)<sup>65-68</sup> direct 5-HT<sub>1A</sub> agonists such as 8OH-DPAT,<sup>69-71</sup> and by direct agonists for 5-HT<sub>1B</sub> and 5-HT<sub>2</sub> receptors.<sup>70</sup> Similar effects have been reported with MDNM in mice.<sup>72</sup> Furthermore, the effects of 5-HT<sub>1B</sub> agonists on PPI in rats are reproduced by the administration of a 5-HT<sub>1D</sub> agonist in the guinea pig, suggesting a functional behavioral homology in the roles of these receptors across species.<sup>73</sup> This observation further indicates the utility of PPI measures for crossspecies comparisons. The PPI-disruptive effects of 5-HT releasers are prevented by pretreatment with the 5-HT reuptake inhibitor fluoxetine, which prevents the drug-induced release of 5-HT from presynaptic terminals.<sup>65 66 68</sup> The PPI-disruptive effects of direct 5-HT<sub>2</sub> receptor agonists, including hallucinogens such as 2,5-dimethoxy-4-iodoamphetamine (DOI), are blocked by pretreatment with nonspecific 5-



HT<sub>2</sub> antagonists<sup>70</sup> or the selective 5-HT<sub>2A</sub> antagonist MDL 100907,<sup>71</sup> but not by a 5-HT<sub>2C</sub> antagonists<sup>75</sup> or by the DA blocker haloperidol.<sup>74</sup> The 5-HT<sub>2A</sub> antagonist is also effective in blocking the effects of 5-HT releasers on ppl.<sup>74</sup> Such findings have contributed to the current investigation of MDL 100907 as a putative nondopaminergic antipsychotic in patients with schizophrenia.

### **Using PPI in Models for Neurodevelopmental Processes Relevant to Schizophrenia**

Sensorimotor gating deficits in schizophrenia patients, unlike PPI deficits in apomorphine-treated rats, are not an acute drug response, but instead reflect longitudinal and complex interactions of genetic, developmental, social, and environmental forces. For this reason, it is important that startle gating in rats appears to be sensitive to these same forces. Studies indicate that developmental perturbations significantly alter PPI in rats. For example, recent studies<sup>76</sup> indicate that isolation-reared rats exhibit a neuroleptic-reversible deficiency in PPI compared to groupreared controls. This effect of isolation rearing appears to be developmentally specific, in that similar isolation of adult rats failed to produce the deficit in PPI observed in isolation-reared rats.<sup>77</sup>

These studies of the effects of isolation rearing on PPI have been extended significantly by Varty and Higgins.<sup>78</sup> In their studies, significant reductions in PPI produced by isolation rearing were reversed by typical antipsychotics (haloperidol, raclopride), atypical antipsychotics (clozapine), and risperidone. Our preliminary findings support the sensitivity of this paradigm to atypical antipsychotics, including olanzapine and seroquel (Geyer, Bakshi and Swerdlow, unpublished data). Thus, PPI deficits in isolation-reared rats may be a valuable paradigm that-like the apomorphine-induced disruption of PPI-is sensitive, but not specific, in its ability to identify compounds with atypical antipsychotic properties.

In one finding of direct relevance to neurodevelopmental theories of schizophrenia,<sup>79</sup> we have noted impaired PPI and

enhanced sensitivity to the PPI-disruptive effects of apomorphine in postpubescent rats that had received neurotoxin lesions of the hippocampus as neonates.<sup>80</sup> It will be important to identify the peripubertal neural circuit changes that occur in neonatal hippocampal-lesioned rats and that are responsible for the development of this supersensitive DA-mediated loss of PPI in adulthood. Thus, using strategies that involve either manipulations of the rearing environment or neonatal limbic cortical circuitry, PPI studies can potentially be used to examine the contribution of developmental processes to the pathophysiology of sensorimotor gating deficits in schizophrenia, and to identify compounds with potential atypical antipsychotic properties.

### **Using PPI in Genetic Studies: Strain Analyses and "Knockout" Strategies**

Genetic factors may also be critical determinants of sensorimotor gating in rats, since strain-related differences in the dopaminergic modulation of PPI have been reported.<sup>81</sup> Others have begun to systematically characterize differences in startle response properties in 46 different rat strains.<sup>82</sup> If susceptibility to the gating-disruptive effects of DA agonists is genetically controlled in rats, these studies might offer critical insight into genetic factors mediating the susceptibility to and development of schizophrenia in humans.<sup>79</sup>

Several new lines of investigation have advanced our understanding of the genetic regulation of PPI. One strategy applied by Ellenbroek and associates<sup>83</sup> utilized pharmacogenetic inbreeding to produce strains of rats that were either sensitive (APO-SUS) or insensitive (APO-UNSUS) to the behavioral effects of apomorphine. Male and female rats were identified from each generation who exhibited the most (APO-SUS) or least (APO-UNSUS) grooming in response to 1.5 mg/kg apomorphine. Within a single generation, APO-SUS rats exhibited significantly less PPI than did APO-UNSUS rats. Rats were also studied that were part of a longstanding breeding program in which APOSUS and APO-UNSUS rats were inbred for multiple generations. PPI was measured



in rats from the 17th and 18th generations of this breeding strategy. Rats descended from an inbred APO-SUS strain exhibited significantly less PPI compared to rats descended from an inbred APO-UNSUS strain. Apparently, the physiological substrates that regulate the behavioral sensitivity to apomorphine (presumably some feature related to DA receptor sensitivity) are associated with substrates that regulate PPI, and which are transmitted genetically. APO-SUS rats have elevated numbers of striatal D<sub>2</sub> receptors,<sup>84</sup> and increased responsivity of both the hypothalamic-pituitary adrenal (HPA) axis<sup>85</sup> and dopaminergic systems.<sup>84</sup> Certainly, the inheritance of reduced PPI might reflect the expressed inheritance of any one, or a combination of several, of these characteristics.

The use of PPI paradigms in mice has received recent attention, in part because of the advances in molecular biology that rely on murine models. In mice, robust PPI is readily demonstrated, as is a wide range of pharmacological effects on ppl.<sup>72</sup> Using a classical genetic approach, Bullock and colleagues<sup>86</sup> have begun to study inheritance patterns of PPI characteristics. In these preliminary studies, PPI was compared among seven mice strains, and the strains with the highest (C3H/2Ibg) and lowest (DBA/2J/Ibg) levels of PPI were inbred. A quantitative analysis of inheritance revealed that PPI, but not startle amplitude per se, followed a pattern consistent with dominant transmission. Similar approaches are currently being applied to examine the genetics of PPI in families of patients with schizophrenia.

Another genetic strategy has recently been applied to understanding the normal physiological substrates regulating ppl.<sup>87</sup> PPI was compared between wild-type mice (VM mice) and mice that had been genetically engineered to lack serotonin-1B receptors, so-called 5HT<sub>1B</sub> "knockouts" (5-HT<sub>1B</sub>-KOs). PPI was significantly reduced in Vv7 mice by the 5HT<sub>1A/1B</sub> agonist RU24969, but RU24969 did not reduce PPI in 5-HT<sub>1B</sub>-KOs. This experimental approach demonstrates the utility of applying genetic knockout techniques toward understanding the physiological substrates of behaviors and processes such as sensorimotor gating. Similar strategies are currently

being applied toward understanding the dopaminergic substrates of ppl.<sup>88</sup>

## Conclusions

The study of sensorimotor gating deficits in humans and in homologous animal models based on the startle PPI paradigm has already advanced our understanding of possible anatomical, neurochemical, and developmental contributions to information processing abnormalities in psychotic disorders. The advantages of focusing on studies of homologous behaviors that can be quantified in both patients and laboratory animals in the development of an animal model have facilitated the remarkable maturation of this model in less than two decades. While several groups have reported the utility of PPI as a measure that predicts "typical" neuroleptic properties, recent studies suggest that only atypical antipsychotics restore PPI in PCP-treated rats. This model is still relatively new, but findings at least suggest the possibility that the restoration of PPI can be used as a *sensitive* measure (with apomorphine) to identify compounds with both typical and atypical antipsychotic properties, and as a *specific* measure (with PCP) to identify only those compounds with atypical antipsychotic properties. Another variant of this model, examining the ability of compounds to restore PPI in isolation-reared rats, appears to be sensitive to both typical and atypical antipsychotic agents. While the particular behavioral abnormalities being studied in PPI paradigms are not unique to any particular form of schizophrenia or unimodal, the narrowed focus of this work on a specific behavior coupled with the effort to establish and use homologous measures in animals has enabled rigorous studies of both pharmacological and neurobiological influences on sensorimotor gating in rodents that have already prompted clinical tests of novel antipsychotic drugs.

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### Editorial Comments :

Animal models of schizophrenia primarily fall into two categories those that are drug induced and those that do not involve pharmacological interventions. Although each of these models has its own inherent plus points and weaknesses what appears to be quite clear is that no single animal model will capture the various aspects of a complex psychiatric syndrome like schizophrenia. Emerging data from different models hence needs to be carefully examined and synthesized to result in a broader gestalt hypothesis for the pathogenesis of schizophrenia. In addition, drug testing for new pharmacotherapies will likely require testing in more than one model. Amongst the exciting new trends will be the emergence of new developmental and genetic models and as these models emerge the standards to test their validity will also evolve based on a better understanding of the human disorder.

Recent data indicate that there are inherent deficits in prepulse inhibition, a measure of sensorimotor gating, in Brown Norway rats (Palmer AA, Dulawa SC, Mottiwala AA, Conti LH, Geyer MA, Printz MP. Prepulse startle deficit in the Brown Norway rat: a potential genetic model. *Behav Neurosci* 2000 Apr;114(2): 374-88) - these kind of strain differences may suggest this strain as a potential genetic model for schizophrenia. In addition, there is considerable excitement of what will be revealed through the use of either the overexpression or deletion of specific candidate genes in a temporally and spatially controlled fashion. Recent evidence has implicated the cannabinoid receptor gene (CB 1) in the pathogenesis of schizophrenia and CB 1 knockout mice clearly show behavioural alterations which parallel symptoms of schizophrenia. As new loci linked to schizophrenia are revealed the ability to manipulate genes in animal models will greatly aid in the development of new genetic models of this psychiatric disorder.



# Plants Used in the Treatment of Mental Diseases

V. P. K. Nambiar

For most people, today's thoughts include the remorse of yesterday as well as apprehension about tomorrow. People brood upon minor problems until their whole outlook becomes clouded. As a consequence, internal conflicts develop in our daily life. The internal conflicts can lead to the development of stress-related disorders. The situation is so widespread that one out of every three persons is said to be psychologically upset. These psychological imbalances lead to mental diseases of varying intensities. Plants play a great role in treatment regimes to restore the psychological balance.

In *Charaka Samhita*, 10 plants are recommended for restoring memory in mental patients: *Acacia nilotica* (Linn.) Willd. ex Del.; *Picrorhiza scrophulariiflora* (Pennell); *Acorus calamus* Linn.; *Bacopa monnieri* (Linn.) Pennell; *Cynadon dactylon*; *Ferula asafoetida* (Linn.); *Gmelina arborea* Roxb.; *Kaempferia galanga* (Linn); *Nardostachys jatamansi* De.; and *Tribulus terrestris* (Linn).

In addition, *Celastrus paniculatus* Willd., *Clitoria ternatea* Linn. (white flowered) is

reported to be very good for improving memory. For toning up sensory nerves, local physicians use *Bacopa monnieri* (L.) Pennell, *Centella asiatica* (Linn.) Urban, and *Glycyrrhiza glabra* Linn. as single plant remedies. Table I lists 16 plant species which are widely used in 106 Ayurvedic formulations for the treatment of mental diseases.

The methods of application of some Ayurvedic plant preparations are detailed below.

## ***Nardostachys jatamansi* and *Celastrus paniculatus***

The use of *Nardostachys jatamansi* and *Celastrus paniculatus* is very effective in treating mental diseases. A decoction (medicine prepared by boiling powdered root or bark) made out of 10 g of these plants is reported to cure shivering of limbs, sudden convulsions of body, and instability and wavering of the mind. When used as a single plant, only minute quantities of *Nardostachys jatamansi* are needed.

Table 1. Ayurvedic plants and the number of formulations in which they are used.

Plant Name	Family	Formulations
<i>Acorus calamus</i> Linn.	Araceae	24
<i>Allium sativum</i> Linn.	Liliaceae	11
<i>Bacopa monnieri</i> (L.) Pennell	Serophulariaceae	16
<i>Brassica juncea</i> (L.)	Brassicaceae	12
<i>Coscinium fenestratum</i> (Gaertn.) Colebr.	Menispermaceae	21
<i>Curcuma longa</i> Linn.	Zingiberaceae	18
<i>Emblica officinalis</i> Gaertn.	Euphorbiaceae	14
<i>Ferula asafoetida</i> Linn.	Apiaceae	21
<i>Glycyrrhiza glabra</i> Linn.	Papilionaceae	17
<i>Hemidesmus indicus</i> (Linn.) R. Br.	Asclepiadaceae	12
<i>Piper longum</i> Linn.	Piperaceae	25
<i>Rubia cordifolia</i> Linn.	Rubiaceae	10
<i>Santalum album</i> Linn.	Santalaceae	13
<i>Terminalia bellerica</i> (Gaertn.) Roxb.	Combretaceae	14
<i>Terminalia chebula</i> Retz.	Combretaceae	23
<i>Zingiber officinale</i> Rose.	Zingiberaceae	14



### ***Acorus calamus***

The powdered rhizome is used in the treatment of mental ailments. If more than 1 g of powder is given, the patient will start vomiting.

### ***Clitoria ternatea* (white variety)**

The root powder is used for overcoming sleeplessness. A dosage of more than 2 g will lead to loose motion.

### ***Centella asiatica***

The leaves are very good for restoring memory as well as for sharpening memory. In large doses, it produces oversalivation.

### ***Lagenaria siceraria***

The seeds are dried and powdered, and one grain of the powder, if given internally at bedtime, will induce sleep in patients. An oil prepared by using this seed, if applied on the head, will also yield the same result. An oil prepared with the fruit pulp of this species can also be applied on the head.

### ***Withania somnifera* (Linn.) Dunal (Family: Solanaceae)**

- **Distribution:** Throughout the drier parts of India, in waste places, also cultivated.
- **The plant:** An erect branching undershrub reaching about 150 cm in height, usually clothed with minutely stellate tomentum (dense, short, cottony hairs); leaves ovate up to 10 cm long; flowers light yellow in axillary fascicles, fruits globe-like berries which are orange colored, on ripening enclosed in a persistent calyx. The roots are cylindrical-brownish white on the surface and pure white inside.<sup>1</sup>
- **Uses:** The root is used as a nerve tonic and as a sedative for epilepsy and insanity. The root has CNS depressant activity. Chemical studies have been conducted on all parts of the plant.<sup>2</sup>

### ***Rauwolfia serpentina* (Linn.) Benth. ex Kurz (Family: Apocynaceae)**

- **Distribution:** Throughout India as forest undergrowth.

- **The plant:** A small erect shrub or undershrub with red pedicels (stalks with a single flower) and calyx (sepals). Leaves three in a whorl, thin glabrous (without hairs) ' bright green above, flowers white often tinged with violet in irregular corymbose cymes, fruits drupes (fleshy fruit with seeds, surrounded by a strong layer), purplish black on ripening. The roots when dry are very hard, less flexible, tortuous, with a yellowish brown surface with vertical or irregular cracks or wrinkles.<sup>3</sup>

- **Uses:** The root is reported to be an antihypertensive and a tranquilizer. The CNS depressant activity is reported to be present in nonreserpine-containing fractions. Isolation of reserpine and ajmalicine from the roots was carried out in Bangladesh<sup>4</sup> and in France.<sup>5</sup> The root powder (200-500 grams) is given for inducing sleep in mental patients. Continued application of this will sometimes induce clogging of nose, weakness of the lower limbs below the knee, stiffness of the limb joints (especially the elbow), open mouth, and oversalivation. To overcome this, the root powder of *Rauwolfia serpentina* is administered in combination with root powder of *Clitoria ternatea* (white variety) and fruit powder of *Tribulus terrestris*.

### ***Centella asiatica* (Linn.) Urban**

- **Distribution:** Throughout India in moist soil, especially along banks and canals.
- **The plant:** A slender herbaceous creeping perennial with rooted nodes and long internodes; leaves simple with elongated petioles and sheathing leaf bases, broadly cordate (heart shaped), reniform (kidney shaped), crenate (wavy outline), or sinuate (toothed); flowers pink, almost sessile (without a stalk), 3-4 fascicled umbels (umbrella like); fruits laterally compressed with two mericarps (one-seeded portions) having 7-9 similar ridges.<sup>6</sup>
- **Uses:** A decoction (boiled preparation of powdered root or bark) of the plant is sedative and also used for insanity. The leaves are used to improve memory and for



- the treatment of mental disorders. It has CNS depressant activity, antiparkinsonian activity, and improves memory retention. It contains mainly triterpenes, monoterpenes, sesquiterpenes, asiaticosides, flavonoids, and benzenoids. Saponins, sugars, and tannins are also present.<sup>7 8</sup>

***Bacopa monnieri* (Linn) Pennell**  
**(Family: Scrophulariaceae)**

- **Distribution:** Throughout India in wet places up to 1200 m elevation.
- **The plant:** A prostrate or creeping, juicy, succulent, glabrous annual herb rooting at the nodes with numerous ascending branches; leaves simple, opposite, fleshy, obscurely veined; flowers pale blue or whitish, solitary on long pedicels (stalks); fruits 2-celled, 2-valved capsules tipped with style base.<sup>9</sup>
- **Uses :** The entire plant is used as a cardiac, diuretic, anti-inflammatory, and antipyretic tonic and is used as a mental restorative and nerve tonic in the treatment of insanity, epilepsy, and hysteria. It contains flavonoids, triterpenes, miscellaneous alkaloids, and steroids.<sup>10 11</sup>

***Acorus calamus* Linn. (Family: Araceae)**

- **Distribution:** Throughout India in areas up to 1800 m in marshes; also cultivated.
- **The plant:** A semi-aquatic rhizomatous perennial herb, rhizome creeping, much branched, as thick as the middle finger, cylindrical or slightly compressed, light brown or pinkish brown externally, white and spongy within; leaves bright green, distichous (arrangement of leaves where the leaf at one node is opposite to those just above and below it), ensiform (sword shaped), base equitant, thickened in the middle, margins wavy, flowers light brown densely packed in sessile (without stalk) cylindrical spadix; fruits oblong turbinate berries with a pyramidal top; seeds few, pendant from the apex of the cells.

- **Uses:** Dried entire plant is used for cancer in China. It has insecticidal properties and works well against white ants. The aerial parts of the plant are used as an herbal bath for relieving rheumatism and lumbago (pain in the lumbar region). The rhizome powder is used to help smokers quit cigarettes.

- A decoction (boiled root or bark) prepared out of *Acorus calamus*, *Convolvulus pluricaulis*, *Nardostachys jatamansi*, *Bacopa monnieri*, and *Withania somnifera* (12 grams each) is given in two divided doses of 15 ml to treat patients with psychosis. After 6 weeks, the patients show marked improvement.
- The anticonvulsant, CNS depressant, neuroleptic, learning enhancement, and improved memory retention activities of *Acorus calamus* have been reported.<sup>12</sup> Sesquiterpenes, monoterpenes, phenylpropanoids, flavonoids, benzenoids, alkenes, and steroids are the main chemical constituents of this plant.<sup>13</sup>

***Canscora decussata* (Roxb.) Schult.**  
**(Family: Gentianaceae)**

- **Distribution:** Throughout India in moist areas up to 1500 m elevation.
- **The plant:** An erect dichotomously branched annual up to 60 cm in height with 4-winged stems and decussate branches; leaves simple, sessile (without a stalk) up to 5 cm long, prominently 3-nerved; flowers white, those in the fork with long pedicels (stalks); fruits cylindrical, membranous, septicidal capsules.<sup>9</sup>
- **Uses:** Antimycobacterial, analgesic, anticonvulsant, and CNS depressant activities.<sup>14 15</sup>

***Strychnos nux-vomica* Linn. (Family: Loganiaceae)**

- **Distribution:** Throughout India in deciduous forests up to 1200 m.



- **The plant:** A medium sized deciduous tree 15-20 m in height with a fairly cylindrical bole, bark dark gray or yellowish gray; leaves broadly elliptical, coriaceous (with a leathery texture); flowers greenish white in terminal cymes; fruits globose orangered when ripe, containing many discoid, coin-like seeds.<sup>1</sup>
- **Uses:** The root bark has CNS depressant properties. Indole alkaloids are the main constituents of the seeds.<sup>16</sup> The poison, strychnine, is used in homeopathic preparations.

**Abrus precatorius Linn. (Family: Fabaceae)**

- **Distribution:** Throughout India on hedges and bushes in exposed areas.
- **The plant:** A deciduous, wiry climber with tough branches; leaves abruptly pinnate with many pairs of leaflets; flowers pink clustered on tubercles; fruit pods, turgid with a sharp deflexed beak; seeds usually scarlet with a black spot or sometimes pure white.<sup>9</sup>
- **Uses:** Roots, leaves, and seeds are used as a nerve tonic.<sup>17</sup>

**Celastrus paniculatus Willd. (Family: Celastraceae)**

- **Distribution:** Throughout India on hills up to an altitude of 1200 m.
- **The plant:** A large climbing unarmed shrub with long slender elongating branches which are reddish brown and covered with elongate white lenticels; leaves simple, alternate, ovate, crenulate; flowers greenish white in terminal drooping panicles; fruit 3-lobed capsules bright yellow when ripe, seeds covered with orange red aril.<sup>6</sup>
- **Uses:** The essential oil obtained from seeds is used as a tranquilizer. Seeds are used to treat mental disorders. They are reported to increase intellect and memory. Sesquiterpenes, monoterpenes, triterpenes, alkaloids, and lipids are reported to be present in this plant.<sup>18</sup>

**Ginkgo biloba (Family: Ginkgoaceae)**

- **Distribution:** *Ginkgo biloba*, commonly known as maiden hair tree, is a living fossil found naturally growing in the wild in Japan and China.
- **The plant:** In Chinese, it is known as Yin Xing, which means silver apricot. *Ginkgo biloba* belongs to Ginkgoaceae and is the only living representative of the order Ginkgoales. A medium-sized diecious tree with horizontal branches having a pyramidal appearance. Leaves bilobed, more on dwarf shoots and few scattered on long shoots, petiole (leaf stalk) long, venation dichotomous, male strobilus in clusters in the axil of scale leaves on dwarf shoots; the female strobilus is long stalked and borne on dwarf shoots, having two ovules; only one ovule develops into a seed.
- **Uses:** A lot of work has been done on this plant by German scientists. Extract of *G. biloba* has antidementia activity and is good for memory enhancement and learning improvement.<sup>19</sup> The antistress activity of *Ginkgo* was reported by Rapin and associates.<sup>20</sup> *Ginkgo* extracts exert an effect on the veins and venules. It also induces platelet aggregation, slows down the rate of growth of platelet thrombi, and improves the rate of glucose and oxygen uptake in the brain.<sup>21</sup>

The ripe fruits have been used by Chinese in the treatment of tuberculosis, cough, and asthma. A balanced formula of Chinese herbs aimed at life extension contains *Ginkgo*. Several tonics containing *Ginkgo* are sold in the United States as Terrapins Secret, Tebonin, and Roka. *Ginkgo* tonics are called miracle drugs which can forestall aging, improve memory, and optimize brain function.

Many patented drugs containing the plants mentioned above are reported to be beneficial for mental ailments. The patented drugs and their important ingredients are listed in table 2. Which of these is best suited for a particular mental disease is decided by the physician based on his experience.



## Plants Used in the Treatment of Mental Diseases

**Table 2. Patented drugs and their active ingredients**

Sl. No.	Patented drug	Active substance	Manufacturer	Reported claims
1.	Bravobol (capsule)	<i>Celastrus paniculatus</i>	BAN	Brain tonic
2.	Brahmi vita	<i>Centella asiatica</i>	Sandu	Nervous disorders
3.	Brahmi vita (capsules)	<i>Withania somnifera</i> <i>Centella asiatica</i> <i>Asparagus racemosus</i> <i>Nardostachys jatamansi</i> <i>Canscora decussata</i> <i>Tribulus terrestris</i> <i>Elettaria cardamomum</i>	DAP	Memory, sleep, mental calmness, and ability
4.	B-Vite (tabs)	same as above	DAP	Memory, sleep, mental calmness, and ability
5.	Brento (tabs)	<i>Canscora decussata</i> <i>Centella asiatica</i> <i>Withania somnifera</i> <i>Glycyrrhiza glabra</i> <i>Acorus calamus</i> <i>Rauwolfia serpentina</i> <i>Myristica fragrans seeds</i>	Sandu	Nerve tonic
6.	Jyothish Brahmi (Lehyam)	<i>Acorus calamus</i> <i>Celastrus paniculatus</i> <i>Xylia xylocarpa</i> <i>Plumbago indica</i> <i>Pterocarpus marsupium</i> <i>Syzygium caryophyllatum</i> <i>Embelia ribes</i> <i>Terminalia chebula</i> <i>Eclipta prostrata</i> <i>Emblica officinalis</i>	Sanco	Improves memory
7.	Siledin (tabs)	<i>Rauwolfia serpentina</i> <i>Canscora decussata</i> <i>Eclipta prostrata</i> <i>Centella asiatica</i> <i>Holostemma ada-kodien</i> <i>Acorus calamus</i>	Alarsin	Sound sleep, Good for epilepsy, headache
8.	Alert (capsules)	<i>Celastrus paniculatus</i> <i>Acorus calamus</i> <i>Canscora decussata</i> <i>Nardostachys jatamansi</i> <i>Eclipta prostrata</i>	Vasu	Induces calmness
9.	Nurogin	<i>Rauwolfia serpentina</i> , <i>Nardostachys jatamansi</i> <i>Boerhaavia diffusa</i> <i>Tinospora cordifolia</i> <i>Acorus calamus</i> <i>Tribulus terrestris</i> <i>Asparagus racemosus</i>	Herbo	Good for mental agitation and nerve disorders
10.	Mentat (tab)	<i>Centella asiatica</i> <i>Withania somnifera</i> <i>Nardostachys jatamansi</i> <i>Celastrus paniculatus</i> <i>Terminalia chebula</i> <i>Emblica officinalis</i> <i>Mucuna prurita</i> <i>Terminalia arjuna</i> <i>Acorus calamus</i>	Himalaya	Good for all mental activities



Table 2. Patented drugs and their active ingredients (continued)

Sl. No.	Patented drug	Active substance	Manufacturer	Reported claims
11..	Transina	<i>Withania somnifera</i> <i>Ocimum tenuiflorum</i> <i>Tinospora cordifolia</i> <i>Picrorhiza scroplulariiflora</i> <i>Eclipta prostrate</i>	Day's	For all kinds of stress and strain
12.	Vitesson	<i>Withania somnifera</i>		Invigoration

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# Ayurveda: Chemical Constituents of Some CNS Active Plants: Their Importance

N. Anand

Ayurveda, even though very ancient in its origin, continues to be widely practiced in India. This is largely due to its having a sound theoretical base and a well-established Materia Medica. Ayurveda, during its formative period (800 B.C. to 700 A.D.) did not have available to it the experimental-analytical capabilities of the modern sciences, and after this period, due to a variety of factors, it withdrew into a shell. The interaction of the modern sciences with Ayurveda should, therefore, be viewed from a different angle than merely to provide new drugs. This interaction should also contribute to the theoretical basis of a system that has provided an alternative approach to health care and cure of diseases for so long. Thus, the importance of the knowledge of the chemical constituents of the CNS active plants used in Ayurveda should not be only for the development of new drugs (whether as such or through the structural leads provided), but also to provide a modern scientific explanation for Ayurveda theories, doctrines, and postulates. Further, the quality-control procedures and methods of preparation and manufacture of Ayurvedic drugs could be upgraded based on this knowledge. The chemical constituents of some of the more important CNS active plants used in traditional system drugs are discussed in this article from these perspectives.

## The Road Map to Modern Therapeutics

The routes of many of the modern therapeutic agents can be traced back to the plants used in ancient societies. In countries which had highly developed civilizations (e.g., China, Greece, and India) with well-developed indigenous systems of medicine having a sound theoretical basis, their use got incorporated into the materia medicas of

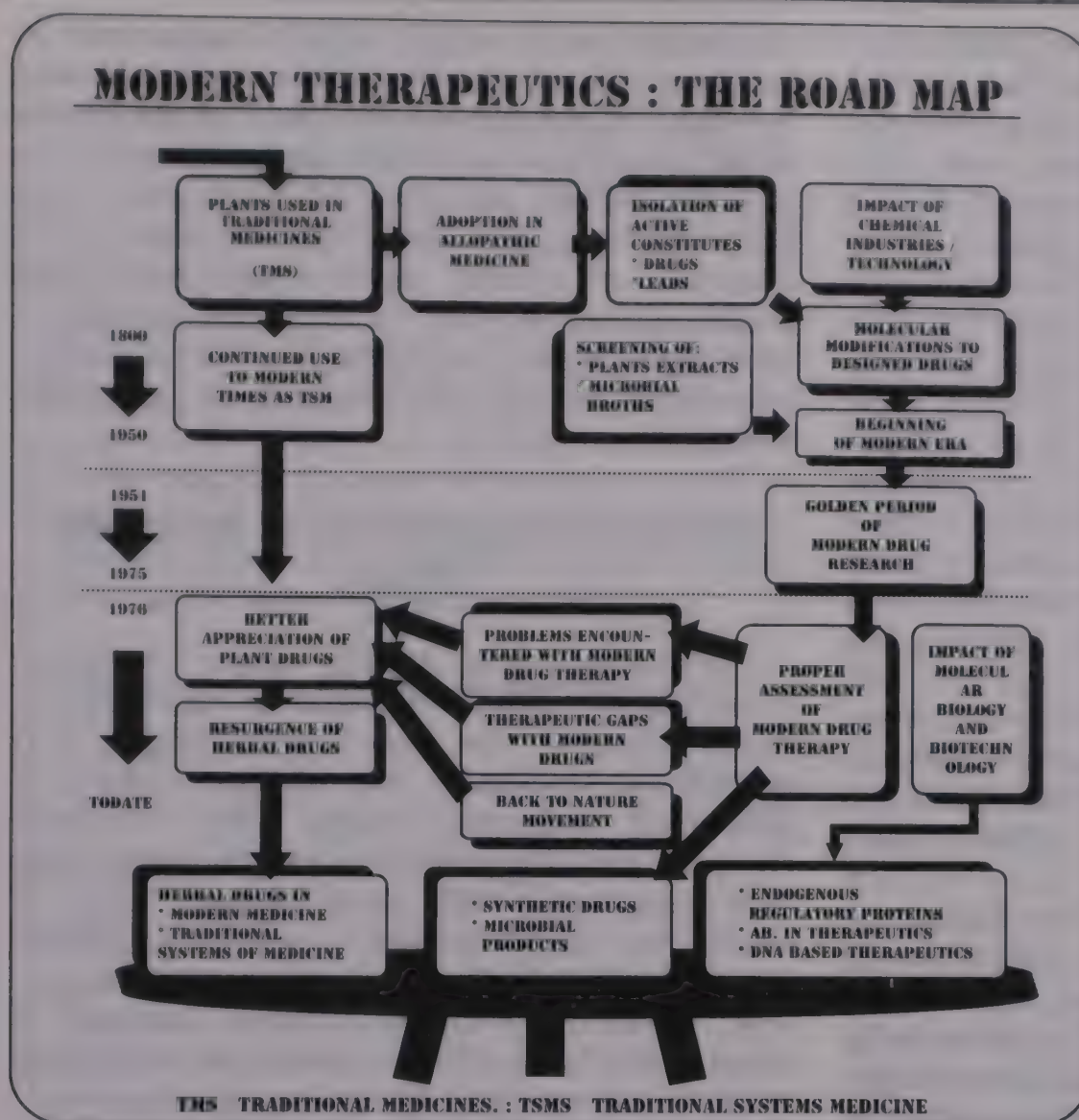
these systems of medicine. These systems or their variant forms spread to other regions of the world. As modern science progressed, two streams or routes followed, which are illustrated in figure 1.

One stream of Greek medicine resulted in the development of the allopathic system in Europe. The allopathic system adopted the use of many of the herbal drugs of these ancient systems. The story of this stream from then on is quite well known and is schematically shown on the right half of figure 1. The use of plant products (or traditional system drugs) was gradually overtaken by that of synthetic drugs and microbial products till about the mid- 1970s when, due to a variety of reasons, a reappraisal of modern medicines versus those of traditional medicine gradually set in. The main reasons for this were the undesirable side-effects of a number of modern drugs; some therapeutic gaps with modern drugs; disenchantment with industrialization; and a back-to-nature movement; nonavailability and unaffordable cost of allopathic drugs for large cross-sections of people in developing countries. In addition, natural products are recognized as one of the most important sources for generation of molecular diversity, which forms the sheet anchor of new drug discovery. Due to these and some other factors, interest in the use of plant products in therapeutics has emerged.

On the other hand, in countries where these plant drugs were used as part of well-developed systems of medicine, such as in China and India, their use has continued almost uninterrupted into the modern era. As modern sciences developed primarily in the Western industrialized countries and were considered alien, indigenous systems of medicine were kept aloof from them. This was one reason why Ayurveda did not benefit from the impact of modern scientific developments.

Many attributes are common to Ayurvedic and allopathic systems. For example, both are





**Figure 1.**

based on the hypothesis that the curative and disease-causing agents are different, as opposed to homeopathy, and both accept the importance of the scientific/experimental approach. Of course, there are some basic differences as well. Ayurveda is holistic and integrative in its approach to health and disease, while allopathy is deductive and segmented. There are perhaps historical reasons for this. Ayurvedic concepts evolved at a time when the cellular and molecular structure of matter was not known and so were primarily speculative and philosophical. Now the two streams are converging; allopathic medicine is developing holistic and integrative concepts, while Ayurveda needs to become more analytical and integrate the holistic view of the healthy body with the cellular and molecular understanding of human and animal systems.

It is most appropriate that the two streams are now meeting, and an interface of the two is being considered important to achieve

"Health for all." This brings up some important issues. What are the strengths of Ayurveda, in theory and practice, which have been responsible for its continued practice for almost 3000 years? Whatever survives in nature must have some inherent survival advantages. There is need to evolve approaches to understand Ayurveda theories in the context of modern scientific developments. Considering the sociopharmacoeconomics of drug usage, it is important to develop an interface between Ayurvedic and allopathic medicine therapeutics.

This reassessment of the potentials of the Ayurvedic and allopathic streams is necessary. It is an emerging view that the two could be complementary in many ways and supplement each other.

In some of the therapeutic gap areas and particularly in chronic ailments, depending largely on host-response, Ayurvedic drugs may be particularly useful. Similarly, for minor non-life-threatening or chronic ailments, the pharmacoeconomics may be in favor of the use of Ayurvedic drugs.

### Ayurveda Today

Ayurveda, though ancient in its origin (around 700 B.C.) continues to be widely practiced in the Indian subcontinent. More than half of the population in this region use the Ayurvedic system for their health care needs, some because of the lack of easy access to modern drugs but many by deliberate choice on account of their faith in this system. In India, there is organized teaching and training of the Ayurvedic system, more or less on the same pattern as for the modern allopathic system.<sup>1</sup> There are around 100 graduate training medical schools, 25 postgraduate institutes, and departments with an annual outflow of about



2,500 Ayurveda graduates. There are around 1,500 Ayurveda hospitals, 12,500 registered dispensaries, and about 300,000 registered Ayurvedic practitioners (vs. 700,000 in the allopathic system in 1990). However, during the formative period of its development, Ayurveda did not have available to it the knowledge base and experimental-analytical capabilities of modern sciences. Further, due to a variety of reasons from around 700 A.D. onward, Ayurveda withdrew into a shell, and the impact of modern developments in cognate sciences was minimal. Although the theories and concepts were based on a scientific approach and methods, Ayurveda did not adopt the analytical framework of modern sciences and remained primarily observational and philosophical. Similarly, its materia medica has lacked the analytical precision which the techniques of modern chemical sciences can provide.

This situation existed until the beginning of this century, when the techniques of modern sciences started being applied to Ayurvedic drugs, with inputs particularly from modern chemistry and pharmacology. However, these efforts were directed primarily toward the development of modern drugs from the Ayurvedic materia medica and not toward contributing to the development of the science of Ayurveda. The knowledge of the chemical constituents of active plants and therapeutic products used in the Ayurvedic system is important, not only for the development of new drugs but also to provide a physiological and physicochemical basis for the doctrines and principles of Ayurveda. Knowledge of the chemical constituents of Ayurvedic drugs should help us to understand, in physiological terms, the unified Ayurvedic holistic view of health and disease and its control and cure.

Ayurvedic drugs are most often composite fractions of plants or even mixtures of a number of plants and therefore contain a number of chemical constituents. The use of these may partly be for historical reasons, since chemical separation techniques were not available when these drugs were developed. But Ayurvedic physicians also very often used composite drugs deliberately and were aware of the concepts of synergism,

modulation of activity of one component by another. A knowledge of the structure and function of individual chemical constituents would provide a scientific explanation of the pharmaceutical practices of Ayurveda. This knowledge would also help in developing methods of quality assessment (and thus enable better quality control), in modifying and modernizing methods for the manufacture, and in the effective use of Ayurvedic drugs.

### **Chemical Constituents of Ayurvedic Drugs**

Characterization of the active chemical constituents would provide a chemotaxonomic criteria for the identification and quality assessment of plants used for preparing Ayurvedic drugs. The chemical composition of a plant can vary substantially depending upon the place, season, time of collection, and storage conditions, which would in turn affect its therapeutic value. The classical pharmacognostic method of plant identification is not adequate and would need to be replaced by chemotaxonomic criteria.

Characterization of the active chemical constituents would provide useful tools to examine the theory and doctrines of Ayurveda and to promote interactions between Ayurveda and allopathic medicine. Detailed pharmacological studies with chemical constituents of active plants would be useful to examine the theoretical bases of Ayurvedic doctrines. This point is elaborated later.

Characterization of the active chemical constituents would provide marker(s) for developing quality-control standards for Ayurvedic drugs. It is most important to develop quality-control standards for Ayurvedic drugs to ensure batch-to-batch uniformity. Individual chemical constituents or a fingerprint of different chemical constituents could serve as useful markers for this purpose. The marker(s) need not be only the active constituent but could be one or more of the major chemical constituents. These constituents could be measured quantitatively. Standardization of extracts is a must for ensuring reproducible activity.



Characterization of the active chemical constituents would provide quality-control standards for modernizing and upgrading the methods of production. Once the quality control markers are known, these can be used to modernize production methods while ensuring quality control.

Characterization of the active chemical constituents would provide leads for the development of new drugs for the allopathic system of medicine. It is quite well known that the origins of many of the drugs used in the allopathic medicine can be traced to the active chemical constituents obtained from Ayurvedic or other traditional drugs.

### Rasayana Drugs of Ayurveda

Some concepts are special to Ayurveda, and one such concept is that of health promoters, termed Rasayanas (rejuvenators or tonics).<sup>2 3</sup> According to Ayurveda, drugs are of two types: those that cure disease and those that promote health and prevent disease. Rasayanas belong to this latter category.<sup>3</sup> The multifactorial actions of Rasayana drugs are to provide a feeling of well-being, promote natural resistance to stress and diseases, improve mental acuity and memory, prevent aging and degenerative diseases, accelerate anabolism and stimulate metabolism, restore health and increase lifespan, and rejuvenate sexual functions.

It is likely that all of the Rasayana plants and their chemical constituents do not exhibit all these activities. Isolating the different chemical constituents and studying their different activities would help in understanding the total or combined action of these plants much better.

It would help to understand whether these constituents are acting alone or in concert. It is likely that some of these plants (or their chemical constituents) are acting as immunomodulators and stimulating the nonspecific resistance component of the immune system. The action of Rasayana drugs is likely to extend to different systems and organs in the body from the immune system to the CNS, cardiovascular system, and gastrointestinal tract.

There is an interesting parallel to this in

contemporary immunology research. It has been shown that conditioning in animals leads to an enhancement of the natural killer cell activity.<sup>4</sup> There is increasing evidence for a bidirectional communication between the nervous, immune, and endocrine systems: T-lymphocytes have  $\mu$  opioid receptors; CD4-T cells can produce methionine-enkephalin;<sup>5 6</sup> opiate addicts have an increased incidence of infections and cancers; and in animals, opioids have been shown to be immunosuppressive.<sup>7</sup> Muramyl peptides, which are structural units of bacterial cell walls, were earlier found to exhibit marked immunostimulant activity.<sup>8</sup> Later they were also shown to be somnogenic.<sup>9</sup> More recently, we have observed that N-palmitoyl-MDP, an analog of MDP, which is a strong immunostimulant and provides protection against parasitic infections, is also an adaptogen,<sup>10</sup> thus pointing to a link between the immune and neuronal networks.

The action of Rasayanas also seems to cut across different systems and organs in the body. *Panax ginseng*, widely used as a tonic in traditional Chinese medicine and more recently as an adaptogen, has been shown recently to also be an immunomodulator and to protect against Semliki Forest Virus infection by enhancing the effect of interferon inducers.<sup>11</sup> It would be useful and interesting to study the action of Rasayana drugs and their chemical constituents, singly and in concert, on the neuroimmune axis.

### CNS Active Plants in Ayurveda

In Ayurveda, drugs acting on the nervous system are classified into a number of categories, the more important of which are given below,<sup>12</sup> along with their nearest equivalents in the modern pharmacological classification.

- Apasmarhara: antiepileptic
- Medhya: intelligence and memory promoting
- Madakari: addictive/narcotic
- Nidrajanana: hypnotic/sedative
- Rasayana: rejuvenators, adaptogens,



- antistress agents
- Samjnasthapana: resuscitative
- Vamanopaga Chardi, Nigrahana Vamanopaga: emetic and antiemetic, respectively
- Unmadahara: to cure insanity

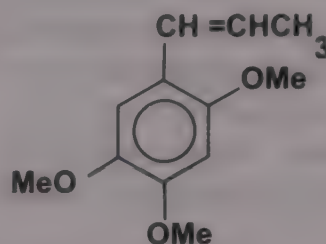
A number of drugs (around 85) are classified in Ayurveda under these categories, and many under more than one category.<sup>12</sup> Some of the more commonly used drugs have been experimentally investigated, and their chemical constituents are well characterized. Eight of these are described below. These are used either as single drugs or as components of compound drug preparations.

Two plants, *Ginkgo biloba* and *Valerian jatanmansi*, are included although they do not belong to the tradition of Ayurveda. These plants are included because of their long tradition of use as CNS drugs. *Ginkgo biloba*, although of Chinese origin, has been intensively studied recently in Germany and France. Both plants are clinically used mainly in pharmaceutical forms that are very close to the general approach of Ayurvedic therapeutics, as a composite fraction so that the different chemical constituents can add to or modulate each other's effects or activities.

Each plant is described in a tabular form with appropriate references under each heading, which will make for easy reading. The plants are listed according to their botanical names, while the indigenous name is given in parenthesis. The head "Traditional Uses" includes those mentioned in Ayurvedic texts, while "Used in Ayurvedic Practice for" includes its uses in current clinical practice.

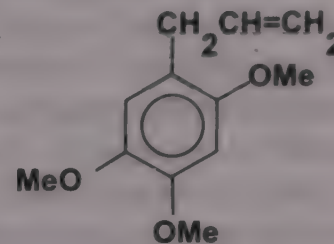
#### **Acorus calamus (Vacha)**

- *Parts used*: rhizome
- *Traditional uses*: in disturbed conditions of Vata and Kapha
  - Sedative, insomnia
  - Epilepsy and hysteria
  - Nerve tonic; to promote intellect and intelligence
  - Major active chemical constituents<sup>13</sup>



$\alpha$ -Asarone (E Isomer)

$\beta$ -Asarone (Z Isomer)



$\gamma$ -Asarone

- *Pharmacological activity*
  - Essential oil exhibited depressant,<sup>14 15</sup> anticonvulsant, and antispasmodic actions.<sup>16</sup>
  - Asarones showed tranquilizing activity, prolonged ethanol and barbiturate sleeping time, and anesthetic activity,<sup>17</sup> prevented depletion of adrenal ascorbic acid in cold stress,<sup>18</sup> and did not cause any change in norepinephrine content of the whole brain of rats.<sup>19</sup>
  - $\alpha$ -Asarone potentiated the effect of reserpine and chlorpromazine<sup>20</sup> and produced a prolonged calming effect in monkeys.<sup>18</sup>
  - Aqueous and ethanol extracts have been proposed for treatment of petit mal epilepsy.<sup>21</sup>
- *Standardized on the basis of*:
  - Asarone content
- *Clinically used in Ayurvedic practice for*:<sup>22</sup>
  - Mental disorders as a tranquilizer or sedative
  - Epilepsy
  - Enhancing memory and mental performance

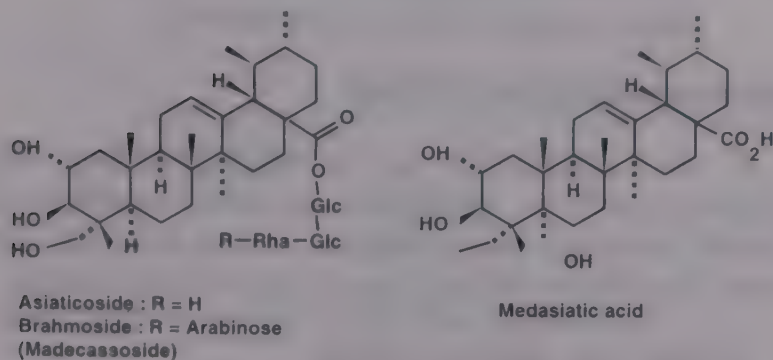
#### **Centella asiatica; Syn. Hydrocotyl asiatica (Brahmi; Mandukaparni)**

It is one of the important Rasayana plants of the Ayurvedic system (to enhance mental performance) and also of the folk medicine of Madagascar, where it is used mainly for skin infections such as for leprous sores.

- *Parts used*: whole plant
- *Traditional uses*:<sup>12 23</sup>



- Memory enhancer
  - Mental disorders: insanity
  - Wound healing; antileprotic
- Headaches



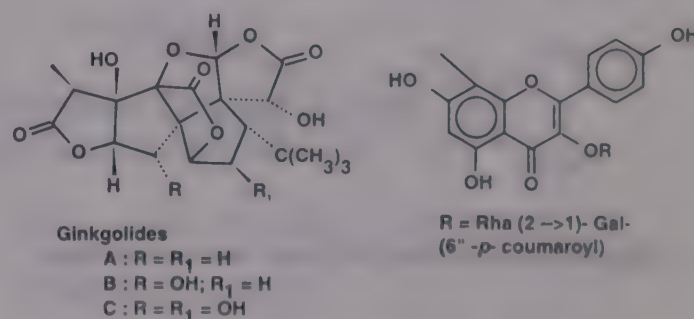
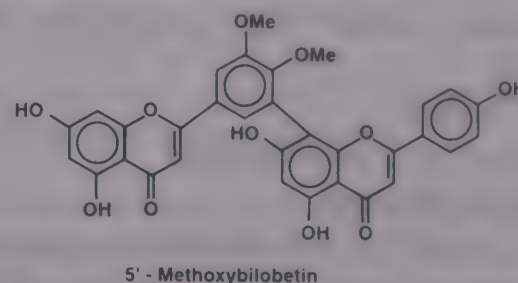
- Major active chemical constituents<sup>24 25</sup>
- Pharmacological activity
  - Alcohol extract exhibited CNS depressant action, caused sedation and hypothermia, potentiated barbiturate hypnosis, had anticonvulsant action, exhibited D2 dopamine receptor antagonist action and cholinomimetic action blocked by atropine and chlorpromazine.<sup>26 27</sup>
  - Prevented cold-induced gastric ulcers in rats.<sup>28</sup>
  - Aqueous extract decreased spontaneous motor activity, had anticonvulsant action, and appeared to have an anxiolytic action.<sup>29</sup>
- Clinical trials
  - The dried herb showed significant intellectual and behavioral improvement in mentally retarded children.<sup>30</sup>
- Clinically used in Ayurvedic practice for:<sup>12 30 31</sup>
- Mental disorders, as sedative and tranquilizer
- Improving mental performance and behavior, especially in children
- Nerve tonic
- Chronic venous insufficiency and for cellulitis
- Wound healing

### Ginkgo biloba (maiden-hair tree)

Ginkgo is regarded as a living fossil, since

it can not be found wild in the world. Extract from Ginkgo is one of the most important recent additions to herbal medication and has become Germany's most commonly prescribed herbal medicine.

- Parts used: leaves
- Traditional uses:<sup>32 33</sup>
  - Cough and allergic inflammation
  - Circulatory disorders
  - Headaches
  - Age-related problems
  - Memory and learning
- Major active chemical constituents<sup>33-35</sup>



- Pharmacological activity<sup>32 33 36-38</sup>
  - Ginkgolide-B: a potent and specific platelet activating factor (PAF) antagonist, used as a reference compound for PAF receptors in biological systems.<sup>37</sup>
  - Extract: vasodilator both peripheral and central; antioxidant; inhibits prolactin secretion from cultured rat pituitary cells.<sup>38</sup>
- Standardization:
  - Leaf extract standardized on the basis of flavonoid content; Ginkgolide-B detected by LC-MS.
- Clinically used for:<sup>32 39-42</sup>
  - Cerebral and peripheral vascular insufficiency, restores regional cerebral blood flow after embolism
  - Age-related problems, memory and learning; improves behavioral and



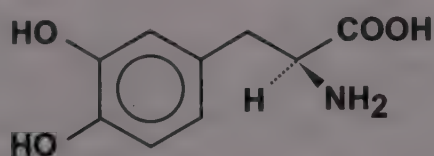
mental performance; antidementia and 'nootropic'

- Free-radical scavenger
- Tinnitus and hearing loss
- Ginkgolide-B for treatment of severe sepsis and for prophylaxis of asthma

### ***Mucuna pruriens* (Kawaanch)**

This plant is a good source for the production of L-dopa; depending upon the source and quality of the seeds, yields of 1.54 percent have been reported.

- *Parts used:* pods, seeds
- *Traditional uses:*<sup>43</sup> for conditions affected by Vata
  - Male virility
  - Tremors and convulsions
  - General debility
  - More recently as antiparkinsonian drug<sup>44</sup>
- *Major active chemical constituents:*<sup>45</sup>



L-dopa and some derivatives and precursors

**Pharmacological activity:** Seed powder shown to exhibit:<sup>46</sup>

- Antiparkinsonian and hypothermic activity in experimental animals equivalent to L-dopa but with faster onset of action.
- Increased motor activity in mice.
- Reversed apomorphine-induced hypermotility in mice unlike L-dopa.
- Inhibited chlorpromazine-induced hyperprolactinemia.
- Unlike L-dopa, the seed powder did not significantly potentiate the epinephrine response in haloperidol-treated dogs.

These results suggest that the seed powder resembles L-dopa in its action on dopaminergic pathways, but has perhaps other constituents which contribute to the improved antiparkinsonian activity and greater tolerability in animals.

- Clinically used in Ayurvedic practice for:<sup>42-47</sup>

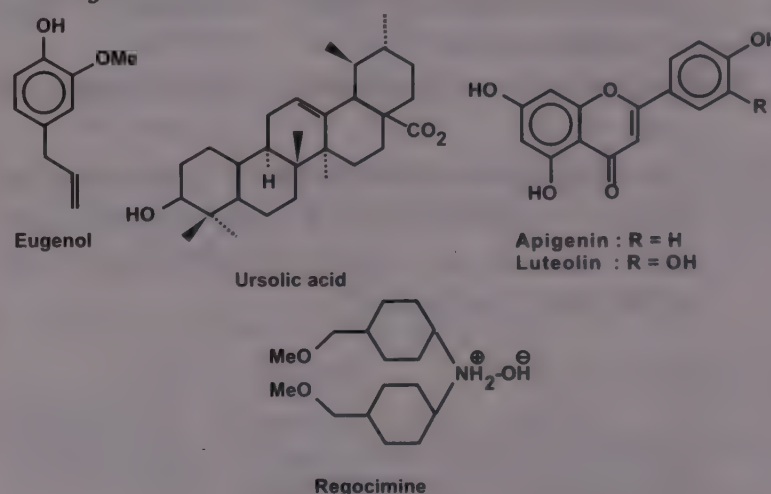
- Parkinsonism
- Hyperprolactinemia
- Improving mental performance

### ***Ocimum sanctum* (Tulsi)**

It is considered as a sacred plant by Hindus and is planted in the traditional Hindu houses for worship. It is one of the most important Rasayana drugs of Ayurveda.

- *Parts used:* leaves, seeds
- *Traditional uses:*<sup>48</sup>
  - Stress-related imbalances
  - Skin diseases
  - As a health promotor (Rasayana drug)
  - Antipyretic
  - Expectorant for bronchitis
  - Antiemetic

- *Major active chemical constituents:*<sup>49-51</sup>



- *Pharmacological activities:*<sup>52-55</sup> Leaf extract:
  - Potent adaptogenic and antistress activity, increase in brain level of succinate dehydrogenase (SDH); immunomodulator, immunostimulant, almost equipotent to Panax ginseng, with a better safety margin<sup>52-53</sup>
  - Liberates ACTH from primary cultures of rat pituitary cells
  - Hepatoprotector<sup>54</sup>
  - Prevents stress-related rise of 5-HT and decrease of MAO and of catechol amines in the brain of rats<sup>55-56</sup>



• **Clinical studies:**

- Ocimum leaf powder reported to improve hypertension in 50 cases of stress-related essential hypertension and in cases of viral encephalitis.<sup>57-58</sup>

• **Clinical uses in Ayurvedic practice:**

- Health promotor and to improve mental performance
- For chemoprophylaxis of viral infections, cancers, and parasitic infections

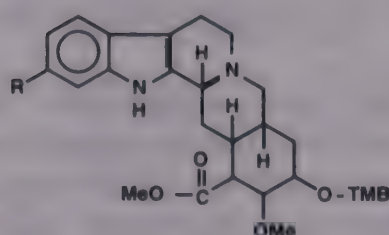
**Rauwolfia serpentina (Sarpagandha)**

• **Parts used:** roots

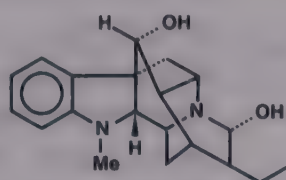
• **Traditional uses:**<sup>59</sup> In conditions caused by an imbalance of Vata and Kapha

- Insanity and insomnia: as a sedative/hypnotic
- Epilepsy
- Snake bite

• **Major active chemical constituents:**<sup>60-63</sup>



Deserpidine : R = H  
Reserpine : R = OMe



Ajmaline

• **Pharmacological activity:**

- Total extract and reserpine exhibited antihypertensive, tranquilizing and antipsychotic activities
- Ajmaline exhibits antiarrhythmic and antihypertensive activities

• **Clinical studies:**

*Rauwolfia serpentina* has been very extensively studied almost since early 1920s when modern drug research methods were applied to the investigation of traditional system drugs. Early clinical studies in India with the crude drug and its extracts established the antipsychotic (tranquilizing) and antihypertensive activities of this drug.<sup>64-69</sup> During this period, some of

its major alkaloids, including Ajmaline, were isolated in India.<sup>60</sup> However, it was the isolation of reserpine (by Ciba, Basel scientists) in the early 1950s,<sup>61</sup> which has very potent hypotensive and tranquilizing activities, both in animals<sup>62</sup> and in clinical studies, which established the clinical value of this plant. This was a big event in modern drug research, which sharply focussed world attention on traditional systems, plants as sources, and leads for new drugs. Reserpine or a standardized powder or total extract of the roots were widely used in modern clinical practice for many years; many physicians preferred to use the crude drug/ total extract and claimed a better therapeutic effect and safety margin.

• **Therapeutic uses in Ayurvedic practice:**

- For mental disorders, insanity
- For insomnia
- For epilepsy

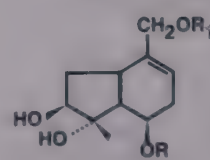
**Vateria wallichii: Syn. Vohicinalis/jatamansi**

• **Parts used:** rhizomes and roots

• **Additional uses:**<sup>70</sup>

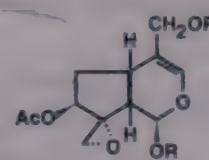
- Sedative, tranquilizer
- Epilepsy and hysteria
- Nervous and emotional stress

• **Major active chemical constituents:**

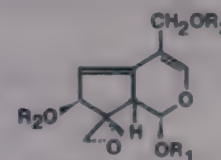


Valerioside

- 1 : R = Glc; R<sub>1</sub> = isovaleryl  
2 : R = isovaleryl; R<sub>1</sub> = Glu



Dihydrovaltrate  
R = isovaleryl



Valtrate  
(R<sub>1</sub> = R<sub>2</sub> = isovaleryl  
R<sub>3</sub> = Ac)  
(Valpotriates)

**Pharmacological activity:**<sup>71-79</sup> Valerian extract *in vitro* causes:

- Inhibition of the breakdown of  $\gamma$ -aminobutyric acid (GABA)
- Interaction with the GABA-benzodiazepine-chloride channel receptor complex<sup>72</sup>

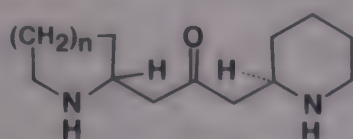
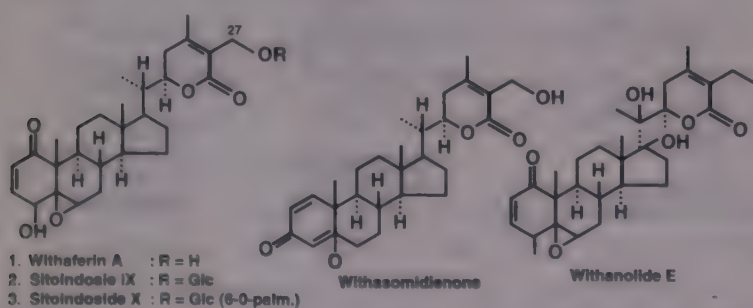


- Behavioral and EEG changes<sup>77-79</sup>
- Cytotoxic activity against colon, lung, and cervical cancer cell lines
- **Standardization:**  
There is no strict correlation between the activity of the extracts and the content of valepotriates, but their content can be used as a marker for quality control.<sup>81</sup>
- **Clinical results:**  
In previously untreated epileptic patients, sodium valproate monotherapy showed progressive improvement in attention, immediate recall, intelligence, and visuospatial functions.<sup>80</sup>
- **Clinically used for:**<sup>81-83</sup>
  - Sleep disturbances and loss of alertness
  - Mental disorder: as sedative, tranquilizer
  - For delirium and epilepsy
  - For inflammation and arthritis

### ***Withania somnifera* (Ashwagandha)**

It is one of the important Rasayana drugs of Ayurveda and is used as a Medhya Rasayana.<sup>81</sup>

- **Parts used:** roots
- **Traditional system uses:**<sup>84</sup>
  - To attenuate cerebral function deficit in geriatric population, antiarudety
  - To augment learning and memory
  - To improve nonspecific host defenses (Rasayana drug)
  - To treat ulcers
- **Major active chemical constituents:**<sup>85-87</sup>



- **Pharmacological activity:**<sup>88-91</sup>
  - Total alcoholic extract showed sedative and tranquilizing activity, decreased acetylcholine (ACh) and catecholamine levels, and increased 5-HT and histamine levels in brain
  - Total alkaloid fraction showed prolonged hypotensive and respiratory stimulant action
  - Visamine potentiated barbiturate time, caused hypothermia, and exhibited nicotinolytic action.
  - Withaferin A and withanolide E had immunosuppressive and antitumor action.
  - Sitoindosides IX and X showed immunostimulant and antistress activities in experimental animals, enhanced learning, acquisition and memory retention in both young and old rats, influenced monoamine oxidase (MAO) metabolism in brain, and appear to affect GABA-ergic mediation and inhibit the activity of acute phase reactants during inflammatory process and bring about reduction in  $\alpha$ -2-macroglobulin synthesis.
  - Sitoindosides VII-X and withaferin A reversed ibotenic acid induced cognitive deficit and the reduction in cholinergic markers<sup>91</sup> (models for learning and memory).
- **Clinical results:**
  - Clinical trials in patients with anxiety revealed significant reduction in the level of anxiety and improvement of mental functions.<sup>92-93</sup>
  - Ashwagandha is widely used in Ayurvedic clinical practice, both as a single drug and in combination with other reputed plant drugs; two such composite preparations have recently been described.<sup>94-96</sup>
- **Clinically used in Ayurvedic practice for:**
  - Old-age problems, geriatric tonic, memory enhancer
  - Alzheimer's disease
  - Antistress activity
  - Inflammatory and arthritic problems
  - Alleviating adverse effects of morphine



and associated depression.

- Management of patients on drugs of abuse.

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# Contemporary Drug Development in the United States: Bridging the Gap

D. E. Nichols

Contemporary drug development in the United States has changed dramatically in recent years. Managed care and increased regulation of prescription drug prices in managed care settings has forced the major pharmaceutical firms to downsize in order to maintain profitability. Mergers of numerous individual firms, followed by downsizing and restructuring, have led to larger corporations that presumably have more efficient infrastructure and management. It is also perceived that larger firms with greater resources are necessary because of the rapidly escalating costs of new drug discovery, now estimated to be in excess of \$300 million, as well as the increased time for regulatory agency approval for most drugs. As a consequence of these pressures, there is a compelling need to improve both the speed and the effectiveness of drug discovery.

## Traditional Drug Discovery-Natural Product Sources

There is presently a resurgence of interest in identifying drugs from natural sources. Both terrestrial and marine organisms are being intensely examined, the motivation being based at least in part on the fact that many species are being driven to extinction by the activities of man. It is hoped that useful plant species can be quickly identified before they are lost forever.

In the past at least, natural products served as important leads for drug discovery. One could cite as notable examples digitalis, quinine, morphine, atropine, curare, cocaine, and the ergot alkaloids. A formalization of this process, bioactivity-directed fractionation, is represented in figure 1. A plant with a known biological effect is extracted and the extract subsequently fractionated. The fractions are then assayed for a biological effect resembling the crude plant product. The active fraction is then analyzed, its main

component isolated and purified, and its structure determined.

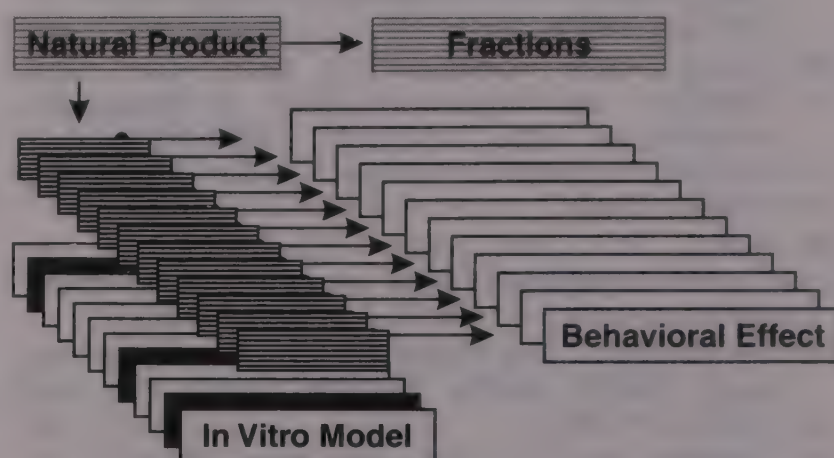


Figure 1. A Schematic for bioactivity-directed fractionation of a natural product with CNS effect. In this model, there is one major active component in the natural product that possesses activity, both in simple models and in whole animal pharmacology.

This approach has led to a variety of different drug types. Nevertheless, the number of useful therapies derived from natural sources, as a percentage of all extant species on the planet, is very small. It must also be kept in mind that these drugs were not identified through a process of random screening, which is very inefficient, but were isolated from plants with a rather long history of folkloric use, often being initially recognized for their extremely toxic properties (e.g., atropine from belladonna). In most cases, this knowledge was accumulated over millennia, the actual discovery of the properties of the plants being lost in antiquity. This knowledge base has been nearly completely exploited in something less than 200 years! At least in Western civilizations, plants that are believed to possess therapeutic effects that have not yet been investigated are vanishingly few in number, and it is often the case today that the rationale for investigating particular species is weak or even nonexistent; there is much more random screening than in the past.



## The Contemporary Process of Drug Discovery

The contemporary process of "drug discovery" for small molecules can be envisioned as occurring through one of four different approaches:<sup>1</sup>

1. Modification of a lead structure
2. Screening of compound inventories in disease model(s)
3. Modification of natural enzyme substrates or receptor ligands
4. *De novo* design, usually computer assisted

If one considers these points one by one, certain limitations are evident. Thus, in the first approach above, one requires a lead molecule to initiate the drug discovery process. Structural modifications of a lead compound would routinely be carried out during the process of lead optimization, often a statistically driven computer-based approach. Drug discovery would occur in this context during the lead optimization process, when structural modification leads to a compound with an unexpected type of biological activity. This process, of course, is predicated upon the assumption that a lead of some sort is in hand, and begs the question as to the origin of the lead. Similarly, in the other three activities, it is assumed that adequate models of the disease state exist, or that a specific biological target for the therapeutic agent has been well defined.

Although lead structure modification *may* result in unexpected new types of biological

activity, the objective of lead modification more generally is to obtain molecules that possess optimal therapeutic properties (lead optimization). Thus, lead optimization is more properly considered to be drug development, as shown in figure 2, rather than drug discovery.

In the second case, one does not initially require a lead molecule but instead must have a specific disease model that can be employed in a high-throughput screen. In the case of combinatorial libraries, which are very much in vogue today, one may require the evaluation literally of tens of thousands of molecules in a particular screen. "Hits" obtained during the screening process potentially represent lead compounds, amenable to lead optimization.

The third type of approach to drug discovery is built upon two assumptions: (1) knowledge of the natural enzyme or receptor that must be targeted for a successful therapeutic outcome and (2) the ability to design successfully some derivative or analog of the natural ligand that takes advantage of the target in an appropriate way. Assuming that one knows whether an agonist (substrate) or antagonist (inhibitor) for the macromolecule is required, the essential knowledge to direct the design of a useful ligand is often lacking.

The activity listed in approach 4 represents the most formidable process of all. *De novo* design requires not only that one be able to identify the key biological target, but also demands that one understand in an intimate way all the factors involved in the ligand-macro-molecule interaction so that these can

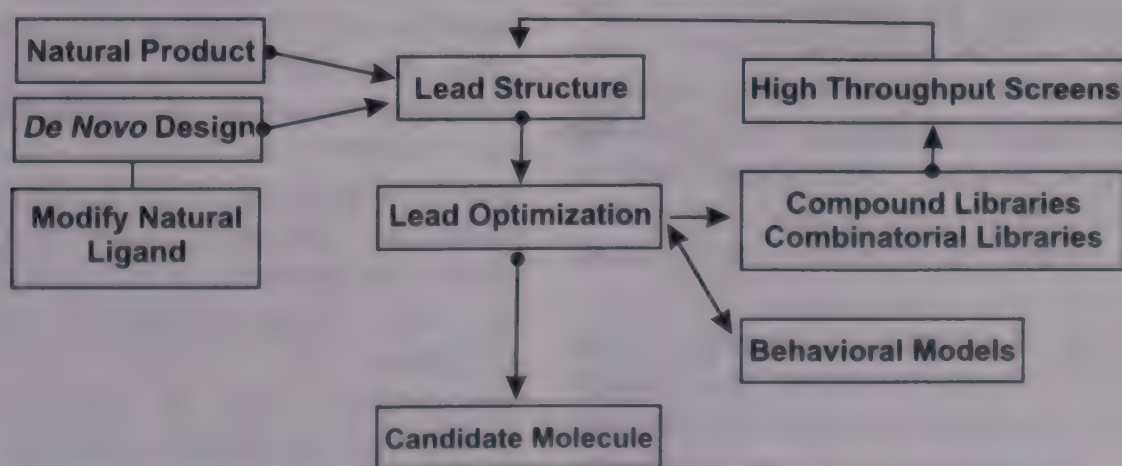


Figure 2. A general flow chart for contemporary CNS drug development



be designed into the molecule as required.

Of course, even when a particular molecule exhibits a promising profile of biological activity *in vitro* or in model systems, if the processes of absorption, distribution, metabolism, and excretion are unfavorable, they may render the substance useless as a therapeutic agent.

As medical science begins to appreciate the complexity of various systems that modulate key peripheral processes such as regulation of blood pressure or heart rate or renal function, it is often possible to identify specific biological targets for therapeutic intervention. Control of blood pressure, for example, may be approached with one or more of a variety of different pharmacological agents, including alpha- and beta-adrenergic receptor blockers, peripheral vasodilators, diuretics, converting enzyme inhibitors, and angiotensin receptor antagonists. For each drug, a biological target is readily identifiable. For any of these particular targets, as noted in point 2, models exist, and compound libraries can be rapidly screened. A drug company needs merely to specify which of the particular targets is of interest, develop high-throughput assays to model them, and then screen in-house or combinatorial libraries. If a lead structure can be identified, rational drug design processes can usually be invoked to optimize the desirable properties of the lead.

Although *de novo* design is still rare, one could consider the recent development of HIV protease inhibitors as an example of that approach. While the design of this highly exciting class of enzyme inhibitors was initiated with an actual lead molecule identified by screening, the final compounds were designed based on knowledge of the structure of the enzyme obtained from x-ray crystallographic studies.<sup>2</sup> An understanding of how these inhibitors bound to the protease molecule allowed further structural refinement in an iterative fashion, resulting ultimately in inhibitors with very high affinities.

To summarize the general process that applies for a great many diseases, one would: (a) identify a key biological target; (b) develop models for the target that are amenable to high-throughput screening; (c) screen available compound libraries or combinatorial

libraries; (d) identify a lead compound with at least modest activity in the model assay; and (e) optimize the lead, either through rational drug design or "recycling" back through combinatorial chemistry with the lead structure as a starting point.

### CNS Drug Discovery

The development of therapies for schizophrenia and other mental disorders is more problematic because specific biological targets are less well identified or understood, or may even be completely unknown. Indeed, CNS drug development is completely dependent on a model that ideally possesses face validity, simplicity, and economy. One could safely argue that the availability of an appropriate model is the major limitation on CNS drug development. Many models bear the name of the drug they were designed to mimic, rather than a disease state, with activity for new compounds described (at least initially) with terms such as "cocaine-like," "atropine-like," or "chlorpromazine-like." In fact, models for CNS disorders have been developed based largely on the knowledge of how current therapies work. For example, because most neuroleptic agents disrupt conditioned-avoidance responding (CAR) in the rat, the ability of a new substance to elicit this effect has been taken as an indication that the drug may have an antipsychotic action. Thus, for example, one hears of the ability of a drug to disrupt the CAR, rather than its possessing an antipsychotic action in rats, the latter being an unwarranted anthropomorphic leap.

For nearly all CNS drugs, the drug action was discovered in man rather than an animal model. This again relates to the fact that models are usually developed after the fact, and are derivative of an already known therapeutic agent. It might also be mentioned that models as typically employed are often used to help identify pure compounds. For example, the discovery of reserpine as the active component of *Rauwolfia serpentina* and its brief employment in the treatment of schizophrenia in the early 1950s was based on historic use of *Rauwolfia* in India for treatment of certain mental disorders.<sup>3</sup> The fractionation of *Rauwolfia* using models, however, led to pure reserpine, which unfortunately also had the propensity to



produce severe mental depression, an effect not recognized as characteristic of the whole plant preparation. Pure reserpine as a therapeutic agent was thus soon displaced by the phenothiazine antipsychotic chlorpromazine, the drug that is credited with beginning a revolution in the treatment of mental illness.

The utility of chlorpromazine in the treatment of schizophrenia was discovered serendipitously,<sup>4</sup> as no biological target had been envisioned beforehand. Chlorpromazine served as the lead compound in further and extensive drug development efforts. When it became clear that the therapeutic efficacy of the phenothiazines was highly correlated with the ability to antagonize dopaminergic function, this pharmacological effect became the model used for further drug development.

The discovery of the phenothiazines was soon followed by the introduction of butyrophenones such as haloperidol, also a serendipitous discovery that arose from studies of meperidine-type analgesics. The butyrophenones proved to be even more selective antagonists of dopamine function. With the advent of radioligand competition experiments, and the later subdivision of dopamine receptors into  $D_1$  and  $D_2$  subtypes, it was found that  $D_2$  antagonist properties appeared to be essential to the antipsychotic effect of the neuroleptics. At that point, the ability to act as an antagonist at the dopamine  $D_2$  receptor became the model for further antipsychotic drug development. A mind set ensued that, in the absence of the discovery of new antipsychotic agents with novel mechanisms of action, has generally precluded the development of therapies for schizophrenia that are not based on dopamine receptor blockade. Indeed, the "dopamine hypothesis" of schizophrenia has largely dominated thinking about treatment approaches.

Recently, clozapine has gained acceptance as an antipsychotic, despite its tendency to cause agranulocytosis, because it has a lower incidence of extrapyramidal side-effects than other agents (i.e., it is an atypical antipsychotic agent) and because many schizophrenics who are resistant to other antipsychotic agents do respond to clozapine. An examination of the receptor binding profile

of clozapine revealed that it had higher affinity for dopamine  $D_4$  than for  $D_2$  receptors, and in addition, that it had high affinity for serotonin 5-HT<sub>2</sub> receptors. These findings prompted pharmaceutical companies to initiate drug development programs aimed at potential atypical antipsychotic agents with novel receptor binding profiles incorporating antagonist activity at dopamine  $D_4$ ,  $\alpha$ -adrenergic, or 5-HT<sub>2</sub> receptors, as well as molecules possessing antagonist activity at both 5-HT<sub>2</sub> and  $D_2$  or  $D_4$  receptors.

The altered dopamine receptor selectivity profile for clozapine has led to a reexamination of the importance of the various dopamine receptor subtypes in the actions of antipsychotic agents.<sup>5</sup> The importance of 5-HT<sub>2A</sub> receptors in modulating dopaminergic effects has also been reassessed, leading to the introduction of risperidone, a mixed  $D_2$ /5-HT<sub>2</sub> antagonist, as well as MDL 100,907,<sup>6</sup> a potential antipsychotic agent that is a specific 5-HT<sub>2A</sub> antagonist with no appreciable dopamine receptor blocking activity.

It is fairly clear that the serendipitous discovery of chlorpromazine and haloperidol, and the recognition of their dopamine antagonist properties, has led to a path of drug discovery and development that until very recently has deviated little from the dopamine hypothesis of schizophrenia. Dopamine receptor subtypes are being thoroughly explored to determine whether better therapeutic agents may result from isoform-specific antagonists, but there is little significant effort directed toward the examination of receptor systems other than for dopamine.

### **Discovery of Novel CNS Active Agents**

The preceding discussion is meant primarily to illustrate how lead structures (chlorpromazine, haloperidol) have driven drug development and discovery for antipsychotic agents. Not only have lead structures driven the drug discovery process, but their pharmacology has clearly driven theories of mental illness. These processes are so tightly coupled that there has been little reason to develop novel antipsychotic agents that do not target dopamine receptors as one component of their action.



Is this situation desirable? Can one be absolutely certain that aberrant dopamine pathways are the cause of schizophrenia, or might they be a kind of downstream pathway from the primary lesion(s)? It is certainly possible that other transmitters might be involved in the primary lesion. For example, functional interactions between dopamine and glutamate are well known (e.g., reference 7), and it seems quite possible that disturbances in glutamatergic pathways could lead to CNS affects that might be at least partially ameliorated by appropriate dopaminergic ligands.

Unfortunately, we are not likely to discover these pathways using current drug discovery technologies. High-throughput screens cannot employ behavioral measures and must focus on well-defined receptor or enzyme target systems. These are carefully selected based on their correlation with known and successful therapeutic approaches. In the absence of a lead molecule with novel *in vitro* pharmacology, drug discovery is driven either by known pharmacology or by serendipity. In view of the complexity of the brain, this situation is likely to prevail into the foreseeable future. In fact, this author has previously commented on the low probability that truly novel psychoactive drugs are likely to result from current drug discovery approaches.<sup>8</sup>

Although the class of antipsychotic agents has been used as an illustration, these arguments are just as logically applied to drug classes for other CNS disorders such as depression or anxiety. One solution to this impasse is to identify new leads among natural products with a well-documented history of medical use. Ayurvedic medicine, for example, may hold such leads. If the therapy has been proven efficacious, one has already passed the formidable barriers associated with absorption, distribution, metabolism, and excretion and is presumably dealing with a medicine possessing activity at a specific molecular target. The question to be asked is whether this site is one that is already recognized or whether it is completely novel. The isolation and structure elucidation of the active principle(s) from a natural product, followed by conventional receptor screening technologies, can quickly determine

the answer to this question. If the pharmacological profile is novel and differs from existing drugs, the new agent represents a lead molecule that can serve to initiate the optimization process.

Consider, for example, a clinically effective antipsychotic substance with low affinity for all the subtypes of dopamine and serotonin receptors. How would it be exploited? It would first of all have to be determined whether the drug possessed an antipsychotic profile in behavioral models (e.g., disruption of conditioned avoidance behavior in rats). If the substance was active in this or another behavioral model predictive of clinical activity, the behavioral model could be used to screen second generation molecules, prepared by structural modification, with differing receptor binding profiles until the key pharmacological component was identified. If the behavioral effect proved to be mediated through a specific receptor, this action could then be exploited in high-throughput screens to identify other lead candidates from compound libraries. It would have to be kept in mind early on, however, that the behavioral models might be fundamentally flawed if they are based on currently understood mechanisms of action and might not be useful in the context of a completely novel agent. Indeed, the utility of many behavioral models is that they are correlative with the pharmacology of a series of agents known to have a particular mechanism of action.

If the new lead did not possess activity in a standard behavioral model, drug development could be substantially more difficult. In the event that the lead molecule possessed high affinity for only one receptor type, this in all probability would be the essential pharmacological action required, and one might be safe in assuming that the study of compounds possessing action at that receptor type would serve as an adequate screen for potential clinical candidates. In effect, this idea is what has driven model development for antipsychotic drugs.

If the lead molecule had high affinity for more than one receptor type, lead structure modification would be anticipated to afford a series of compounds with varying affinities at the different receptors. Recalling that this lead molecule fails to show activity in



standard behavioral assays, screening for the desired clinical activity may become quite problematic.

It is also quite possible that novel therapies for mental illness might well be pharmacologically complex. This contrasts sharply with most current trends in the pharmaceutical industry, where pharmacologically *specific* agents are being sought. Consider for example, the case where a whole plant extract might yield several components, none of which can be demonstrated to possess complete activity. Such a situation is presented in figure 3, where fractions are isolated that possess some form of biological activity, but none of them reproduces the effect of the whole plant extract.

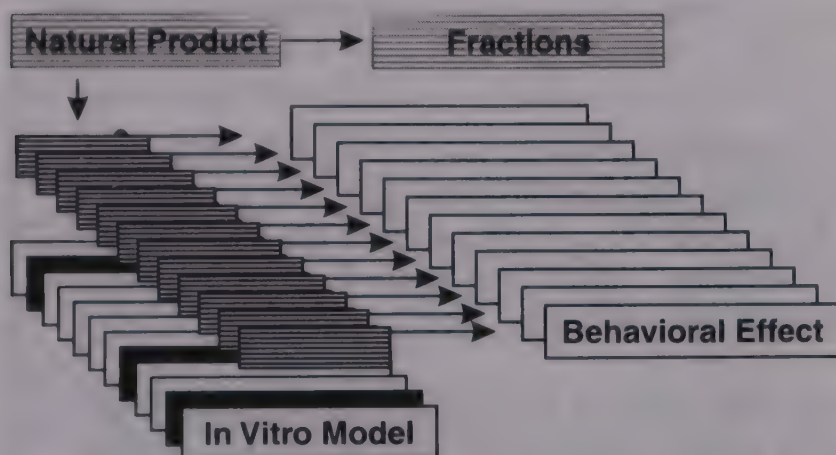


Figure 3. Multiple fractions with in vitro biological activity, none of which reproduces the behavioral effect of the whole plant extract.

An alternative case might be one where a mixture of several plants is used for a treatment, none of which alone is considered to be effective. This is a common situation in Ayurvedic medicine. Extract fractionation of each of the component plants would be analogous to the situation presented in figure 3, where none of the components produces the desired effect. In these examples, one might consider that each of the components produce necessary but not sufficient effects for the complete therapeutic action. It is also possible that one of the components produces the essential pharmacological action, but that one or more other components are synergistic with, or potentiate the action of the essential substance.

Clearly, conventional screening methods and model development will not likely be effective in these examples, and new screening paradigms may be needed. There

may also be models that are presently available but not widely implemented. For example, if one assumes that any significant change in brain neurochemistry leads to a corresponding change in neuronal activity, it should be possible to detect this change in vivo using EEG techniques.<sup>1</sup> Such assays are broad-based, and require no assumptions regarding mechanism of action.

Based on work such as that by Dimpfel and colleagues,<sup>9</sup> complex extracts from natural sources with CNS activity would be expected to produce EEG effects, regardless of their degree of chemical complexity. The salient features of the EEG can be quantitated and known pharmacological agents examined to determine similarities, if any, using patternmatching or neural network approaches. Although the analyses may be complex in the case of multicomponent mixtures, or with single molecules possessing several types of pharmacology, such an assay is not dependent on measuring overt behavioral changes and is not necessarily based on identification of similarity to known pharmacological agents.

Correlation between the receptor-binding profiles of the molecules eliciting an EEG power spectrum with the highest similarity to the lead compound or whole plant extract would presumably lead to identification of the essential pharmacological components. Standard lead optimization techniques could then be used to direct structural modification efforts. Clinical trials would ultimately provide evidence as to whether the isolated pharmacological component was the clinically efficacious one.

Clearly, the identification of novel therapeutic agents for mental illnesses from natural sources is a great challenge. Contemporary drug discovery programs, utilizing highthroughput screens of company libraries, or combinatorial libraries, are *not likely* to lead to truly novel therapies, simply because the assay procedures have been developed based on assumptions about the underlying cause of the illness, for example, the dopaminergic hypothesis of schizophrenia. Natural products used to treat mental illness, with recognized clinical efficacy, represent one of the last obvious sources of truly novel therapeutic agents for



central nervous system disorders. This will continue to be the case until we have a much more detailed understanding of brain chemistry and the underlying bases for various disorders such as schizophrenia and depression.

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## Editorial Comments:

India has Ayurveda as one of the official systems of medicine. Hence, unlike in U.S.A. a team of Vaidyas, psychiatrists and clinical pharmacologists can and do study, directly, the clinical effects of the approved Ayurvedic formulations and plants. Such an approach has been called "Reverse Pharmacology". This has proved to be a cost-effective and productive approach to drug development in India, from Ayurveda.

Several plants used widely in India, showed the clinical experience of activity first. Later the exploratory and experimental projects were taken up by the academia or the industry. The outstanding examples are: (1) the tranquillizing activity of *Rauwolfia serpentina*, (2) the anti-parkinsonian activity of *Mucuna pruriens* (3) the anti-anxiety effects of *Withania somnifera*, (4) the memory and learning-enhancing effects of *Centella asiatica* (5) the hepatoprotective effects of *Picrorrhiza kurroa*, (6) the immunopotentiating effects of *Tinospora cordifolia* etc. The Indo-U.S. projects for the new drug development need to utilize this novel reverse pharmacology approach. Such a clinical emphasis may lead not only to plants and active principle-based new drugs but also to totally new neurodynamic effects. The current animal models are suited for more for the me-too compounds, already in use. Hence only marginal advantages in efficacy and safety emerge from molecular modifications.



# Reporter Summary 3

## Medicinal Aspects of Treatment of Mental Disorders

The session provided an overview of clinical trials of Ayurvedic medicinal substances in mental disorders by Dr. Ramu, a general overview of the preclinical pharmacology of CNS active substances by Dr. Patnaik, and an overview of animal models of psychiatric disorders by Dr. Geyer.

The Ayurvedic unit at NIMHANS has conducted several pilot and controlled studies for assessing the efficacy of herbal drugs used by Ayurvedic physicians in the treatment of different types of mental disorders. Dr. Ramu presented the findings of a double-blind controlled study of Brahmyadiyoga, Tagara, chlorpromazine, and placebo in the treatment of acute schizophrenia (Unmada). Brahmyadiyoga is an herbal preparation consisting of six ingredients: whole plant juice of Mandukaparni (*Centella asiatica*), rhizome powder of Vaca (*Acorus calamus*), root powder of Jatamansi (*Nardostachys jatamansi*), Tagara (*Nymphaea macrosporum*), Kushta (*Saussurea lappa*), and Sarpagandha (*Rauwolfia serpentina*). Brahmyadiyoga and chlorpromazine were found to be better than placebo. No significant differences were found between the other treatment groups - Tagara vs. Brahmyadiyoga, Tagara vs. placebo, Tagara vs. chlorpromazine, or Brahmyadiyoga vs. chlorpromazine.

Dr. Ramu presented the results of several other clinical studies of Ayurvedic treatments that were also conducted at NIMHANS. These studies included clinical assessments of the efficacy of Shodhana (purification) and Shamana (palliative) measures with chlorpromazine in acutely ill patients with Unmada (schizophrenia); Brahmyadiyoga, chlorpromazine, and placebo in patients with chronic schizophrenia (Anavonmada), and Ksheeradhara (a special external purification treatment) in patients with Udvega (anxiety neurosis).

Dr. Patnaik presented a comprehensive overview of the types of preclinical studies that are carried out on novel CNS active compounds or natural products. A preclinical study of a CNS agent typically includes experiments in the following areas: primary and secondary screening, mechanism of drug action, and toxicology. Primary screening tests are carried out to obtain a general activity profile on motor, sensory, and autonomic systems and are typically conducted in rodents. Secondary screening tests are done to determine behavioral activity in animal models of CNS disorders (anxiety, neurodegeneration, dementia, schizophrenia, stress, depression). Secondary behavioral screening is typically carried out in rodents, but some primate models are used. Studies to determine the pharmacological mechanisms of drug action include assays for receptor binding, activity on second-messenger systems, metabolism, turnover, and electrophysiological effects. Toxicity studies include determination of the lethal dose in 50 percent of the animals and teratogenesis, mutagenesis, and carcinogenesis tests in rodents, dogs, or primates.

Dr. Geyer presented an overview of the attributes that confer validity to animal models of human CNS disorders. He then focused on drug-induced deficits in sensory gating as an animal model of schizophrenia. Clinical observations in schizophrenic patients have identified deficiencies in the processing of sensory information, including the inability to automatically filter or "gate" irrelevant thoughts and sensory stimuli from intruding into conscious awareness. Dr. Geyer described his work on the use of the acoustic startle paradigm as a homologous behavioral response found in a number of species from rodents to humans. He has shown that patients with schizophrenia show deficits in prepulse inhibition of the eye blink reflex component of the startle response, that is, they fail to gate or filter incoming sensory



information. Dr. Geyer described studies he has conducted to examine the pharmacological basis of drug-induced deficits in prepulse inhibition of the acoustic startle response in rodents. His findings suggest that the restoration of apomorphine-induced deficits of prepulse inhibition of acoustic startle can be used as a sensitive measure to identify potential antipsychotic compounds with both typical and atypical properties. He also suggests that phencyclidine-induced deficits in prepulse inhibition of acoustic startle can be used as a specific measure to identify compounds with atypical antipsychotic properties.

Dr. Vaidya discussed the need for developing and refining preclinical and clinical tests of natural products with potential CNS activity. He stressed the need for primary and secondary screens for natural products, new animal models of psychiatric disorders in which to test natural products, preclinical dose range-finding studies and kinetic analyses. And such reverse pharmacological studies be directed by clinical studies of natural products in patient populations. Clinical studies can provide new leads for molecules.

### **Plants Used in Ayurveda: Source and Constituents**

The session provided an overview of plants used in Ayurveda, the chemical constituents of plants with medicinal qualities, and an overview of drug discovery and development in the United States.

Dr. Nambiar presented an overview of plants that are used in Ayurvedic medicine. He briefly described the physical characteristics and medicinal properties of 10 plants that are used by Ayurvedic physicians for restoring memory in mental patients: *Acacia nilotica*, *Acacia nilotica indica*, *Acorus calamus*, *Bacopa monnieri*, *Cynadon dactylon*, *Ferula asafoetida*, *Gmelina arborea*, *Kaempferia galanga*, *Nardostachys jatamansi*, and *Tribulus terrestris*. He also described the methods used to collect and prepare the leaves, roots, stems, bark, flowers, fruits, and seeds of medicinal plants such as decoctions (medicine prepared by boiling powdered root

or bark), pastes, and leaf and seed powders and extracts. Dr. Nambiar indicated that multiple commercial preparations and Formulations exist for a number of Ayurvedic plants used in the treatment of anxiety, memory impairment, psychosis, and other mental and emotional illnesses. Many of the plant preparations and their active ingredients are patented in India.

Dr. Nitya Nand discussed multiple benefits that could be obtained by characterizing the active chemical constituents of plants used in Ayurvedic medicine. He indicated that characterization of the active ingredients of medicinal plants would provide (1) chemotaxonomic criteria for the identification and quality assessment of plants used for preparing Ayurvedic drugs, (2) markers for developing quality control standards for Ayurvedic drugs, (3) quality control standards for modernizing and upgrading the methods of production, and (4) leads for the development of new drugs for allopathic medicine.

Dr. Nitya Nand discussed multiple uses of Rasayana drugs (health promoters, rejuvenators, or tonics) used in Ayurveda to provide a feeling of well-being, promote natural resistance to stress and diseases, improve mental acuity and memory, prevent aging and degenerative diseases, accelerate anabolism and stimulate metabolism, restore health and increase lifespan, and rejuvenate sexual functions. He briefly described the parts of the plants that are used, the clinical uses, and the active constituents and known pharmacological activities of several Rasayana plants: *Acorus calamus*, *Ginkgo biloba*, *Mucuna pruriens*, *Ocimum sanctum*, *Rauwolfia serpentina*, *Valeriana wallichii*, and *Withania somnifera*.

Dr. Nichols presented an overview of the time and financial expenditures associated with the development of new drugs in the United States: more than 10 years and approximately \$250,000 to bring a new compound from basic research, through clinical trials, FDA approval, and onto the market for clinical usage. Many compounds have been derived from natural product sources. For example, scopolamine, curare, reserpine, and quinine. Bioactivity-directed fractionation and behavioral assays have been



used to identify the active constituents of plant preparations. The development of specific bioassays such as the HIV protease inhibition assay has allowed for the *de novo* design and high-throughput screening of thousands of compounds for biological activity. In order to be cost-efficient and predictive of potential biological activity, bioassays must be rapid, broad-based, and have face validity.

Dr. Parikh led the discussion of drug discovery from natural products. It was suggested that Ayurvedic physicians should continue to use plant preparations in conjunction with holistic health care. At the

same time, however, it is necessary to identify the active constituents of plant preparations used in Ayurvedic medicine. Chemotaxonomy is one of the first steps in this process. Standardization and quality control of plant preparations, including the time of day, season, and geographical regions in which plants are collected, are needed to standardize the preparation of Ayurvedic drugs. Standardization would also allow clinical trials of Ayurvedic and allopathic medicines to be conducted at multiple sites. The identification and synthesis of chemical constituents of plant preparations will provide leads for the development of new drugs.



# **Indo-USA Workshop on Traditional Medicine and Mental Health**

**National Institute of Mental Health and Neuro Sciences, Bangalore, India  
October 13-17, 1996**

The members of the Indo-USA Workshop collectively formulated the following mission statement to delineate the overall goals and objectives of future Indo-USA collaborative research efforts in the area of traditional medicine and mental health.

## **Mission Statement**

The objectives of the Indo-USA Workshop on Traditional Medicine and Mental Health are to develop mechanisms and to raise resources for a joint Indo-USA research effort focused at multiple levels (cultural, clinical, and pharmacological) on the application of traditional medicine approaches that are used in each culture to improve the clinical diagnosis and treatment of mental illness.

## **Areas Designated for Immediate Action/Implementation**

- Establish a steering group of Ayurvedic and allopathic physicians, pharmacologists, pharmacognosists, social scientists, and behavioral scientists to establish priorities and to begin the implementation of the Indo-USA mission.
- Develop a glossary or lexicon of Ayurvedic terms and concepts.
- Identify appropriate candidates for cross-cultural postgraduate training in biological psychiatry in the United States and Ayurvedic medicine in India.
- Design and implement multicenter clinical trials of Ayurvedic and allopathic treatment of depression.
  - Relevant issues: Research design, criteria for clinical diagnosis, treatment outcome measures, and statistical analysis of treatment outcomes.
  - Reverse pharmacology approach and pharmacoepidemiology.

## **General Recommendations**

Recommendations were made to further the development of Indo-USA collaboration in three major areas of Ayurvedic medicine: cultural and historical research, clinical practice, and psychopharmacology. Specific suggestions within these areas are summarized below.

## **General Aspects of Ayurveda**

- Develop a dictionary of Ayurvedic terms and concepts including those used in the diagnosis and treatment of mental illness.
- Translate Ayurvedic literature pertaining to mental health.

## **Cultural and Historical Research**

- Apply Ayurvedic approaches and perspectives to mental health problems.
  - Develop a standardized clinical interview that would incorporate the (best) key elements of Ayurvedic and allopathic diagnostic approaches, including patient experience and clinician experience (cultural styles and traditions).
  - Address major mental health problems such as aging and drug abuse.
- Study the impact of Ayurveda on family life practices (holistic health care) and on treatment outcomes in mental illness.
  - Treatment outcome measures should incorporate lifestyle, quality of life, and behavior.
  - Case analysis of mentally ill patients; clinical and behavioral profile of patients who are resistant or refractory to Ayurvedic treatment.

## **Clinical Practice**

- Establish a steering group of Ayurvedic physicians, allopathic physicians (biolo-



- gical psychiatrists), pharmacologists, pharmacognosists, social scientists, and behavioral scientists to discuss issues related to the implementation of the IndoUSA mission.
- Establish cross-cultural postdoctoral training in allopathic medicine (biological psychiatry) and Ayurvedic medicine.
- Standardize criteria for diagnosis and treatment of mental illness in Ayurvedic medicine.
  - Define and standardize the components of the *comprehensive Ayurvedic package* which is tailored to individuals (diet, nutraceuticals, pharmacotherapy).
- Standardize Ayurvedic preparations, psychopharmacologic agents, and nutraceuticals used by Ayurvedic physicians in the treatment of mental illness.
  - Identify major plants used in Ayurvedic preparations for the treatment of mental illnesses.
  - Catalog major compounds from known Ayurvedic literature sources (Ayurvedic Pharmacopoeia).
  - Develop standardization protocols using this information.
- Establish multicenter clinical trials of the effectiveness of Ayurvedic and allopathic approaches in the treatment of mental illnesses.
  - Reassess diagnostic criteria of mental illness in Ayurvedic and allopathic medicine. Are we measuring the same emotional, behavioral, and physical elements of the illness?
  - Develop a common protocol for Ayurvedic and allopathic diagnostic criteria. Use International Classification of Diseases guidelines (Chapter V).
  - Develop a common objective rating scale (outcome measures) for the treatment of mental illnesses. Broaden outcome criteria to include social and behavioral measures such as quality of life and integration into society.
- Develop a new clinical research design to evaluate the effectiveness of Ayurvedic and allopathic treatment of mental illnesses. Address statistical analysis of treatment outcome measures.
- Establish multicenter clinical trials of both drugs and nutrients.
  - Use GMP products in clinical trials.
  - Use the Ayurvedic approach to make the preparation and chemical assays to standardize the product.
- First stage trials: clinical evaluation of treatments in depressed patients.
- Second stage trials: clinical evaluation of treatments in schizophrenic patients.
- Study medicated patients who are gradually tapered off drugs rather than use unmedicated or treatment-resistant schizophrenic patients.
- Establish a systematic integration of Ayurvedic and allopathic approaches to the treatment of mental illnesses at NIMHANS or another institution.

### Psychopharmacology

- Animal models: Design novel biological, behavioral, and genetic animal models of mental illness to assess preclinical pharmacology of Ayurvedic treatments.
- Chemotaxonomy: Identify active agent(s) in Ayurvedic plant preparations.
- GMP drug production of Ayurvedic drugs and nutrients: Standardize production of selected Ayurvedic medicines (drugs and nutrients) to be used in multicenter clinical trials in India and the United States.
- Psychopharmacology of Ayurvedic plant preparations: Establish a basic pharmacology program to characterize the mechanism of action of biologically active agents in Ayurvedic medicines.
- Rational drug design: Develop new therapeutic agents for mental illnesses based on active agents in the Ayurvedic pharmacopoeia.



# Glossary of Ayurvedic Terms

**Abhicharaja**-sorcery

**Abhidya**-jealousy, not tolerating the good of others

**Abhikshanam**-out-of-place behavior such as smiling, laughing, singing; a symptom of Vatajon-mada

**Abhimana**-ego; superego and performance of function for achieving the goal

**Abhishapaja**-curse

**Abhyanga**-annointing with oils or an unctuous substance; one of the Cikitsa Sutra (treatment principles)

**Abhyasa**-practice

**Abhyasuya**-cynicism

**Abyasa**-intense study

**Acara** -conduct as defined by social standards and controlled by volition, behaviors

**Acetana**-unconscious

**Acharya**-teacher

**Adbhutadarshana**- showing marvels

**Adhibhautika**-environmental disease, one of three major categories of disease classified according to Sushruta; Sanghatabala Pravritta (trauma induced) condition is an example of the Adhibhau-tika type.

**Adhidaivika**-providential disease, one of three major categories of disease classified according to Sushruta; Kalabala Pravritta (seasonal), Daiva-bala Pravritta (providential), and Swabhavabala Pravritta (physiological) are the three subtypes of Adhidaivika conditions.

**Adhisthana**-seat of origin of a disease; e.g., Manoadhisthana (mind based)

**Adhyatmika**-constitutional disease, one of three major categories of disease classified according to Sushruta; Adibala (genetic), Janmabala (congenital), and Doshabala Pravritta (Doshainduced) are the three subtypes of Adhyatmika conditions.

**Adibala Pravritta**-genetic; classification of disease based on presumed causative factors

**Agantu**-exogenous, refers to the classification of disease according to causation

**Agantu Roga** -a disease having an exogenous etiology due to extraneous factors like injuries, poison, fire, wind; Charaka's classification of disease based on etiology

**Agantuja**-fever induced by extraneous agents such as affliction by Grahās (spirits or deities),

reactions to drugs, poisons, or mental agitations

**Agantuja Unmada** -psychosis induced by extraneous factors such as injuries, poison, fire; a type of Unmada Roga (psychotic diseases) described by Charaka

**Agada Tantra**-toxicology, one of the eight major specialties of Ayurvedic medicine

**Agni**-the digestive and metabolic fire of the body; 13 types are present in the body. When Agni becomes weak, Ama (toxins) accumulate in the body blocking the Srotas (channels of the body or mind); this process triggers Sancaya - accumulation of the Doshas -the beginning stage in the evolution of a disease

**Ahara**-diet; an important aspect of Yuktivya-pashraya Cikitsa (biological or diet-drug therapy)

**Ahara Sakti**-digestive power; part of the tenfold Rogi Pariksha (examination of the patient) to ascertain the individual's state of health

**Aharajanya**-disease states in which food is the causative factor

**Ajasram**-always, not closing, perpetual

**Ajasramatana**-always wandering; a symptom of Vatajonmada

**Akasa** - ether or space; one of the Pancha Mahabhutas-five essential elements of matter; the Pancha Mahabhutas are represented in the psyche of an individual in terms of the Manas Gunas (qualities of the mind, mental constitution)

**Akasmāt Swesham Paresham Abhihananam**-assaultive tendencies; a symptom of Pittajonmada

**Akriti**-facial expression or appearance

**Alasyam**-rest, sleep

**Allopathic medicine**-Western medicine; the treatment of disease by remedies that produce effects opposite to those produced by the disease

**Alpasatva**-weak psyche

**Ama**-toxins or antigenic materials which result when Agni (digestion or metabolic fire) is weak; this triggers an Ama state in which the Srotas (channels of the body or mind) are blocked; an Ama state leads to Sancaya-accumulation of Doshas-the first stage in the evolution of a disease



the evolution of a disease

**Amashaya**-stomach

**Anavasthita Chittatva**-fickle mindedness

**Anidra**-insomnia or sleeplessness

**Anna**-dietetics

**Annavahasrota**-gastrointestinal tract

**AnritaVacana**-telling lies

**Anumana**- logical inference

**Anupasaya** -opposite of Upasaya (drugs, diets, lifestyle)

**Anyatakama**-unlawful sexual activity

**Apasmara** -convulsive diseases; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Apasmara**-epilepsy

**Apatanaka/Apatantraka**-heart disease dominated by Vata; arrhythmia

**Apatantraka** -opposite or irregular action of Vayu  
Aptopadesa-verbal and authentic documentary testimony

**Artha**-wealth

**Asanabilvadi Taila**-a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Asatmyahara**-unwholesome food

**Asatmyendriyārtha Samyoga**-unwholesome contact of sense organs with objects; incompatible physical, verbal, or mental activities; an important factor in the causation of physical and mental disease

**Ashabdashravana**- auditory hallucinations

**Astanga Ayurveda** -the eight clinical specialties of Ayurvedic medicine: Kaya Cikitsa (internal medicine), Salya Tantra (surgery), Salakya Tantra (ear, nose and throat/ophtalmology), Kaumar-abhrtya (obstetrics, gynecology, and pediatrics), Rasayana Tantra (geriatrics), Bajikarana Tantra (sexology), Bhuta Vidya (psychiatry), and Agada Tantra (toxicology)

**Astavidha Pariksa**-eightfold physical examination or general survey of all of the organs by Nadi (pulse), Mutra (urine), Mala (stool), Jihwa (tongue), Sabda (voice), Sparsa (skin), Drk (eye), and Akriti (facial expression or appearance); part of the clinical examination of the patient

**Asthan Amarsh Krodha**- inappropriate anger, violence, or excitement; a symptom of Pittajonmada

**Asthi**-bones and cartilage

**Asuya**-jealousy, envy, intolerance

**Asvagandha**-a drug used in Yuktivyapashraya Cikitsa Withania somnifera

**Asvagandharista**-a compound used in Yuktivyap-

ashraya Cikitsa (diet-drug therapy)

**Asvasana**-assurance therapy; used in Satvavajaya (psychotherapy)

**Aswagandhava Leha**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Aswangandha Curna**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Aswapna**-insomnia

**Atimaithuna**-excessive sexual indulgence

**Atipralapa**-prating

**Atisara**-diarrhea

**Atiyoga**-excessive utilization of Kala (time), Buddhi (intellect), and Indriyārtha (sense organs); an aspect of Prajnaparadha which is considered to be one of the primary causes of disease

**Atma**- soul or spirit

**Atma Bala**-strength and vitality or health of the patient

**Atmabhinivesa**- delusions, paranoia, hallucinations, obsession; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Atmadi Vijnana**- knowledge of the self

**Atmagarana**- excessive wakefulness

**Ausadha, Aushadi**-drugs, medicines

**Ausadhi Dharana**-application of medicines; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)

**Avara Avipakti**-increased peristalsis

**Avritti**- people who have no means of livelihood

**Ayoga**-nonutilization of Kala (time), Buddhi (intellect), and Indriyārtha (sense organs); an aspect of Prajnaparadha which is considered to be one of the primary causes of disease

**Ayu** - life

**Ayurveda**-the wisdom or science of life; Ayurveda encompasses the concept of Swastha, a healthy person, with health defined as a harmony of the mind, senses, and self

**Ayurvedic medicine**-the philosophy of health care dealing with physical, mental, and spiritual health of the individual

**Ayurvedya Manas Roga Vijnana**- rational Ayurvedic psychiatry

**Bacopa monniera**- Bacopa monniera; Brahmi; an herb used as a Ghrita (medicated ghee) and as a Rasayana (tonic) in Yuktivyapashraya Cikitsa (diet-drug therapy); one of the Medhya (memory enhancing) drugs

**Badhas**-afflictions from extraneous agents; treated by Daivavyapashraya Cikitsa (spiritual therapy) ,

**Bahumutra**-frequent micturition

**Bajikarana**-sexology, one of the eight major edic



specialties of Ayurvedic medicine

**Bajikarana drugs**-drugs used for promoting sexology-stamina, virility, and fertility; used as mood elevators in the treatment of depression; e.g., Kapikacchu

**Bala-a** drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Bala Cikitsa**-pediatrics

**Balagrahas**-a disease with convulsions and phobias; thought to be induced by Grahas (deities or planets)

**Bali, Upakara**-oblations or offerings; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)

**Barhi Mamsa**-cuckoo meat; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Basti**-enema; one of the Cikitsa Sutra (treatment principles)

**Bhakti**-desire

**Bhasma, Bhasmas** -a preparation in which minerals such as mica, copper, or zinc are treated with plant juices and heated; herbomineral preparations are commonly used in Ayurvedic clinical practice

**Bhaya**-fear; one of the Manas Dosha Vikaras caused by excessive Bhaya

**Bhayaja**-fear-induced

**Bheda**-one of the six stages in the evolution of disease; the stage of chronicity and complications

**Bhrama**-vertigo; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Bhrama**-giddiness

**Bhuta Unmada, Bhutonmada**- a psychiatric syndrome or set of behavioral alterations named symbolically after the name of a Grahas (planet or deity); a type of Unmada Roga (psychotic diseases) described by Sushruta; this condition is treated primarily by Daivavyapashraya Cikitsa (divine therapy)

**Bhuta Vidya**-psychiatry, one of the eight major specialties of Ayurvedic medicine; it also refers to nonclassical Ayurvedic psychiatry dealing with the management of seizures and other mental disorders induced by Bhutons or Badhas (evil spirits)

**Bhuta, Bhutas** - demons or supernatural beings; thought to be responsible for certain types of psychiatric disorders; e.g., Bhuta Unmada

**Bibhatswam** -loathsome; repulsive, disgusting appearance; a symptom of Kaphajon-mada

**Brahmana**-priests

**Brahmi**-Bacopa monniera; a drug used in Yuktiv-

yapashraya Cikitsa (diet-drug therapy); it is also used as a Ghrita and as a Rasayana

**Brahmi Ghrita** - a medicated ghee prepared mainly with Bacopa monniera; a compound used in Yuk-tivyapashraya Cikitsa (diet-drug therapy)

**Brahmi Rasayana**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy); it contains Bacopa monniera

**Brahmyadiyoga**-a compound used in Yuktivya-pashraya Cikitsa (diet-drug therapy)

**Brahmiyadiyoga**-a compound used in Yuktivya-pashraya Cikitsa (diet-drug therapy)

**Bruyadista Vinasham**-announcing the loss of someone / something dear to the patient

**Buddhi**-decision, thought, intelligence

**Buddhi Mandya**-mental retardation

**Budhim**-learning

**Caturmukha Rasa** - a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Centella asiatica**-Centella asiatica; one of the Medhya drugs; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Cesta**-psychomotor activity, including general motor activity, facial expression, posture, and speech

**Cetana, Puman**-the unification of Satva (mind), Atma (spirit, soul), and Sarira (body) in a human being

**Cetas**-mind

**Chenopodium album**- Vastuka; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Cikitsa**-therapy, treatment, therapeutics

**Cikitsa Sutra**-treatment principles

**Cinta**-anxiety; one of the Manas Dosha Vikaras caused by excessive Cinta

**Citrus medica**-Matulunga; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Citta Vritti**-fluctuations of the mind; Vishayakara

**Citta Vritti Nirodha**- a state of controlled mind

**Cittavasada**-depressive illness

**Cittaviksepa**-disturbed thinking

**Cittodvega**-anxiety

**Cyavanaprasa**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Dainya**-misery; helplessness

**Daivabala Pravritta** - providential; classification of disease based on presumed causative factors Daivavyapashraya Cikitsa-divine or spiritual therapy used primarily in the treatment of Karmik diseases (e.g., Bhutonmadas) which do not respond to Yuktivyapashraya Cikitsa (diet drug therapy); it includes the use of Mantra (incantation), Japa (chanting sacred



incantations), other religious activities, and the wearing of precious stones

**Daivikrita diseases**-diseases caused by evil acts of past life; Karmik diseases; primarily treated by Daivavyapashraya Cikitsa (spiritual therapy)

**Damsatra**-toxicology

**Dasavidha Pariksha** -ten general methods of examination used to assess a person's health: Prakriti (constitution), Vikriti (current state of disease susceptibility or morbidity), Sara (quality of the tissues), Samhana (body build or compactness of the body), Pramana (anthropometry, measurement), Satmya (adaptability), Satva (mental constitution or starnina), Ahara Sakti (digestive power), Vyayama Sakti (physical strength), and Vaya (age and rate of aging); part of the Rogi Pariksha (examination of the patient)

**Decoction**-a medicine or substance prepared by boiling or simmering the leaves, root, seeds, or stems of a plant; a Kashaya

**Deva**-God

**Deva-Guru-Dwija Apamana**-disobedience or disrespect to God, teachers, or learned scholars

**Dhairya**- courage, strong will, self-confidence

**Dhamani**-arteries

**Dhamni Chayascha**-vasodilation

**Dhanwantra Taila**-a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Dhara**-irrigation of the body and head with liquids, hot or cold, allowed to fall steadily from a height, as a continuous dropping which creates a rhythmic movement correcting the course of Vaju and helping to resolve stuck up Doshas; a purification treatment used at Kerala

**Dharma**-virtue, doing good deeds, truth, righteousness, duty, law, justice

**Dhatu, Dhatus**-the seven bodily tissue groups including Rasa (plasma and lymph), Rakta (blood), Mamsa (muscle), Meda (adipose), Asthi (bones and cartilage), Majja (marrow and nerve tissues), and Shukra/Artava (male/female reproductive tissues)

**Dhatu Samya**-restoration of equilibrium or homeostasis; the state of balance of Doshas in the Dhatus (seven bodily tissues)

**Dhi**-intellect- intellectual judgmental faculty

**Dhriti**-resolution; retention of information

**Dhyana**-meditation; used in Satvavajaya Cikitsa (psychotherapy)

**Didoshas**-the mental elements, Rajas (passion) and Tamas (inertia); the Manasika Doshas

**Dinacarya**-the daily code of health conduct; e.g., f

the diet (quality, quantity, and frequency), use of medicated gargles, oil massages, physical exercise; it is part of Swastha Vritta, a comprehensive regimen for maintaining health

**Divaswapnam** -day sleep

**Dosha, Doshas**-elemental substances) of the mind (Manas) and body (Sarira); entities that are capable of vitiating; diseases can be classified based on the predominance of the elements or Doshas involved; the Manodoshas (mental elements) are Rajas (passion), and Tamas (inertia, lethargy); Sariradoshas (physical elements of the body) are Vata (wind), Pitta (bile), and Kapha (phlegm)

**Dosha Dusti**-vitiating or imbalance of the Tridoshas, Vata, Pitta Kapha; Dusti Is the state of vitiating

**Dosha Prakriti**-personality; genetically determined proportion of the three Doshas

**Doshabala Pravritta**-functional; caused by vitiating of the Doshas classification of disease based on presumed causative factors

**Doshapratyaneeka**-anti-Doshic remedy

**Draksa**-grapes; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Dravya, Dravyas**-matter, drugs

**Dravya Guna** -properties of a drug responsible for mediating its therapeutic or pharmacological actions; there are 41 Dravya Gunas classified into four categories: Gurvadi (physicochemical), Par-adi (pharmaceutical), Visista (oriented to the sense organs), and Adhyatmika (psychological)

**Dravya Guna Vigyan** -pharmacology

**Drigviparyaya**-finding fault, misunder-standing

**Drk** - eye

**Dusta Ahara-Vihara, Nidana Sevana**-Pandey

**Dusya, Dusyas**-seven basic tissues of the body which get vitiated by the Doshas (Vata, Pitta, Kapha) during the disease

**Dwayashraya**-dual-type (body and mind dependent) disease, classified according to its Adhithana (base of genesis); examples of Dwayashraya conditions are Unmada (psychosis) and Apas-mara (epilepsy)

**Dwesa**-phobia

**Ekadeshiya Manasikaroga**-one of the two types of Manasaroga (imbalanced state of mind or Manas) as classified by Achal 1976; e.g., emotional excesses such as Kama (desire), Krodha (anger)

**Errhine, Errhines** -medicine prepared with the bile of animals; used in Panchakarma (purification therapy)

**Ersha**-jealousy



**Fomentation**-a hot compress which may contain herbs; an external purification procedure used in Samshodhana (purification and cleansing therapy)

**Gadodvega** - hypochondriasis; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Ghee**-clarified butter

**Ghrita, Ghritas**- medicated ghee (clarified butter) containing herbs or animal products; used in Yuktivyapa-shraya Cikitsa (biological or diet-drug therapy) as an external oleation (oil treatment) and as an Oushada (medicine) in Panchakarma (purification therapy)

**Gnanamagnanam**-knowledge and ignorance

**Go**-cow

**Graha Cikitsa**-spiritual therapy

**Graha, Grahas**-spirits, planets, divinities, deities

**Grahavesa** -psychiatric syndrome or set of behavioral alterations named symbolically after a planet or divinity

**Grahavignana**-psychiatry; Bhuta Vidya; one of the eight branches of Ayurvedic medicine

**Guna, Gunas**-qualities or properties; Manasa Gunas-qualities of the mind, the Trigunas: Satva (clarity), Rajas (passion), and Tamas (inertia); Dravya Gunas-properties of a drug responsible for mediating its therapeutic actions

**Guru**-Preceptor, spiritual teacher

**Harsa, Harsha**- happiness, elation; jubilation; one of the Manas Dosha Vikaras caused by excessive Harsa

**Himsa**-causing injury or torture

**Hinasatva** -people with low mental vitality

**Hita Arthas**-application of the sense organs to wholesome objects

**Homa, Niyama**-sacrifice, vows; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)

**Indriya**-senses, perception

**Indriyabhighraha**-perception and motor control

**Indriyanirapeksha Ayatarthajnana**-delusion

**Indriyartha**- sensory inputs

**Irsha, Irsya**-envy, jealousy; one of the Manas Dosha Vikaras caused by excessive Irsya

**Jala**-water or cohesive factor; one of the Pancha Mahabhutas-five essential elements of matter; the Pancha Mahabhutas are represented in the psyche of an individual in terms of the Manas Gunas (qualities of the mind, mental constitution)

**Jalatrassa**-hydrophobia or rabies

**Janmabala Pravritta**-congenital; classifica-tion of

disease based on presumed causative factors

**Japa**-chanting sacred incantations, etc.; used in Sat-vavajaya Cikitsa (psychotherapy)

**Jars Cikitsa**-geriatrics

**Jara Janya Manas Vikara**-psychiatric problems of the aged

**Jatamansi**- Nardostachys jatamansi; a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Jihwa**-tongue

**Jnana**-knowledge of self

**Jnanendriyas**- sense organs

**Jwara**-fever

**Kakamaci**-Solanum nigrum; used in Yuktivya-pashraya Cikitsa (biological or diet-drug therapy)

**Kala**-time or rhythm

**Kala Parinama**-chronobiological changes occurring in the body as a result of alterations in time factors such as diurnal variations

**Kalabala Pravritta** -seasonal; classification of disease based on presumed causative factors

**Kalyanaka Ghrita** -a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Kama** -passion, desire; sexuality; one of the Manas Dosha Vikaras caused by excessive Kama

**Kamaja**-passion-induced

**Kanthopalepa Bandha**-bronchoconstriction

**Kapha**-phleg,m; one of the three Sariradoshas (physical elements);

**Kapha Prakriti**-the Prakriti (personality) type dominated by Kapha- inhibition is strong and is one with tolerance, power, and Satvik (pure) qualities

**Kapikacchu** -Mucuna pruriens that is used in the treatment of depression and Parkinson's disease

**Kapittha**-wood apple; used in Yuktivyapa-shraya Chikitsa (biological or diet-drug therapy)

**Karma**-actions of past lives

**Karmik diseases**-diseases caused by actions of past life; e.g., Bhutonmadas

**Kasayadhara**-medicines on the forehead; one of the Cikitsa Sutra (treatment principles)

**Kashayn**-a decoction; a medicine or substance prepared by boiling or simmering the leaves, roots, seeds, or stems of a plant

**Kaumarabhrtya**-pediatrics, obstetrics, and gynecology, one of the eight major specialties of Ayur-vedic medicine

**Kaya Cikitsa**-general medicine, one of the eight major specialties of Ayurvedic medicine

**Kevala Manovikara**-mind-based Manovikara (mental disorders) caused by an imbalance in Rajas (passion) and Tamas (inertia); the emotional neurotic disorders; e.g., Krodha



(anger), Lobha (greed); Manoadhisthita Manovikara

**Klama**-neurasthenia; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Kriyakala**-stages in the evolution of a disease; early detection allows therapeutic interventions to restore normalcy

**Krodha**-anger; one of the Manas Dosha Vikaras caused by excessive Krodha

**Krodhaja**- anger induced

**Ksira**-milk; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Ksirabala** -a compound used in Yuktivyapa-shraya Cikitsa (diet-drug therapy)

**Ksiradhara**-irrigation of the body and head (Dhara) with milk; one of the Cikitsa Sutra (treatment principles)

**Kupavasa**-solitary confinement

**Kurma Mamsa**-tortoise meat; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Kushtha**-dermatitis

**Kusmanda**- a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Kusmanda Ghrita**-a medicated ghee prepared mainly with ash gourd

**Kusmanda Pasayana**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Kustha**-leprosy

**Laghutrayi**-the three small books, Madhav Nidana, Sarangdhara Samhita, and Bhava Prakasa; an ancient Ayurvedic text originating from the Vedas

**Laxmivilas Rasa**-Naradeeya; an Ayurvedic formulation commonly used for the treatment of depression

**Lobha**-greed

**Loka**-Universe

**Loka Purusa Samya**-macrocosm-microcosm continuum; the concept that the Loka (universe) and the Purusa (individual) are Panchabhautika (made up of five basic elements) and are in constant interaction with each other; the main principle of Ayurvedic treatment of a disease is to restore harmony between the Loka and Purusa

**Mada**-intoxication, arrogance, euphoria; alcoholism and drug abuse; one of the Manas Dosha Vikaras caused by excessive Mada

**Mada-Murcha-Sanyas**-comas; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Madatyaya**-alcoholism; one of the psychiatric conditions caused by mixed Samprapti (pathogenesis) including both the Sarira (physical Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas

**Mahabhutas, Bhutas**-the basic physical factors or elements making up the mind, body, and the universe

**Mahakalyanaka**-a Ghrita (medicated ghee) used as an external oleation (oil treatment) in Pancha-karma (purification therapy)

**Mahakusmanda**-ash gourd; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Mahapaisachika**-a Ghrita (medicated ghee) used as an external oleation (oil treatment) in Pancha-karma (purification therapy)

**Mahisa Mamsa**-buffalo meat; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Majja**-marrow and nerve tissue

**Mala**-stool

**Malas**-impurities

**Malina** -dirty food

**Malyasyadhikam**-formation or accumulation of impurities (Malas) in excess

**Mamsa**-muscle; meat

**Mana**-pride, emotion, mood, affect; one of the Manas Dosha Vikaras caused by excessive Mana

**Manahkarmavikriti**-impairment of functions of the mind

**Manas**-the mind, perceptual cognitive faculty

**Manas Mandata**-mental retardation

**Manas Prakriti, Manasa Prakriti**-mental or psychological constitution, the quality of consciousness of the mind; there are 16 Manas Prakritis

**Manasa**-mental; diseases are classified as Manasa if there is a predominance of mental abnormalities or symptoms

**Manasa Dosha, Manasa Doshas**-the three Doshas (mental elements)-Rajas (passion), and Tamas (inertia, lethargy); an imbalance in Rajas and Tamas can lead to mental disorders

**Manasa Guna, Manasa Gunas**-qualities of the mind; the Trigunas - Satva (clarity), Rajas (passion), and Tamas (inertia); an imbalance in the Manasa Doshas, Rajas and Tamas, can lead to mental disorders

**Manasa Roga, Manasa Rogas, Manasika Rogaim**-balanced state of Manas (mind) as a result of an imbalance in the Doshas (mental or physical elements); disease conditions in which abnormalities or symptoms are mainly reflected in the Manas (mind); a



disease having a psychological etiology

**Manasika Doshas**-the mental elements, Rajas (passion) and Tamas (inertia); Didoshas

**Manavahasrotas, Maonovaha Srotas** -pathways of the mind; state of mind; it is assessed in the Srotas Pariksa (physical examination of the channels of the body and mind)

**Manda Vihar** -slow body movement; a symptom of Kaphajonmada

**Mandagni** -complains of tastelessness, rejection of food, loss of appetite, reduced food intake; a symptom of Kaphajonmada

**Mandukaparni**-a leaf powder preparation of *Centella asiatica*; used in the treatment of Manas Mandata (mental retardation)

**Mangala**-propitiation; used in Daivavyapa-shraya Cikitsa (spiritual or divine therapy)

**Mani Dharana**-wearing herbs, sacred gems, etc.; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)

**Manoadhithana**-mind-based disease; e.g., Kama (passion)

**Manoadhithita Manovikara (MMV)** - mind-based Manovikara (mental disorders), the emotional neurotic disorders; one of two major types of Manovikara; e.g., Krodha (anger), Lobha (greed)

**Mano-Artha, Mano-Arthas** -functions of the mind such as Chintya (thinking), Vicharya (thoughtfulness), Oohya (discussion), Dheyaya (insight), Sankalpaya (conclusion-drawing)

**Manoashraya**-mind-dependent disease, classified according to its Adhithana (base of genesis); e.g., conditions such as Kama (passion) or Krodha (anger)

**Manodaihika**-mental disturbance in which the condition is manifest as physical signs and symptoms

**Manodaihika Vyadhis**-psychosomatic diseases where the cause of disease is mental and the manifestation is somatic, e.g., Sokatisara (diarrhea of psychological origin)

**Manodosha, Manodoshas, Manasa Doshas**-the mental elements or Doshas: Rajas (passion), and Tamas (inertia, lethargy); the mental constitution of a person is based on the balance of these Doshas; it is believed that an imbalance in Rajas and Tamas can lead to mental disorders

**Manohbighata**-emotional disturbances such as Kama (desire/lust), Krodha (anger), Lobha (greed)

**Manonigraha**-mental control, mind control, selfcontrol; it can be objective as in Satvavajaya Cikitsa (psychotherapy) or subjective as in Yoga

**Manosariradhithita Manovikara (MSMV)** - mind,

body-based Manovikara (mental disorders); the psychosomatic/somaticized neurotic conditions; one of two subtypes of Ubhayadhithita (dual type) Manovikara (UMV); e.g., Jwara (fever), Atisara (diarrhea)

**Manovahasrota Dusti**-the state of vitiation or occlusion of the channels or pathways of the mind, including the sensory pathways

**Manovahasrota Vaigunya**-vitiation of pathways of the mind (Manas)

**Manovikara**-mental disorders

**Mantra** -a mystic word or syllable used in meditation; chanting of hymns (verses with meaning); incantations; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)

**Masthishkalepa**-smearing or anointing on head; application of medications on the head

**Matsarya**-hatred, hostility

**Matulunga**-*Citrus medica*; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Meda**-adipose

**Medhya drugs or Rasayanas** - all central nervous system-active substances or agents which promote or are beneficial to the medha (intellect); brain tonics and adaptogens; nootropic agents; intelligence and memory promoting; e.g., Brahmi

**Medha**-intellect; it encompasses Buddhi (intelligence), Dhriti (concentration and attention), and Smriti (memory); Medhya drugs or Rasayanas promote or are beneficial to the Medha

**Mithayoga**-wrongful utilization of Kala (time), Buddhi (intellect), and indriyarthas (sense organs); an aspect of Prajnaparadha which is considered to be one of the primary causes of disease

**Mithya Vihara**-behavioral excesses

**Moha**- delusion; one of the Manas Dosha Vikaras caused by excessive Moha

**Mohan**-infatuation

**Moksa**-rebirth

**Mukha Sravascha**-salivary hypersecretion

**Murcha**-fainting

**Mutra**-urine

**Mutravahasrota**- urinary tract

**Nadi** - pulse

**Nadi Pariksa**-pulse reading; special method of tactile experience which includes the use of the radial pulse and temporal, carotid, brachial, or femoral pulses; these pulses are related to the vital organs and subtypes of the Doshas (physical elements); there are three basic types of Nadi (pulses) -Vata, Pitta, and Kapha

**Nagadanthi**-*Baliospermum montanum*; an herb



used in Rasayanas (tonics) for purification in longstanding diseases

**Nanatmajavikara, Nanatmaja Manovikara**-disease states caused by an imbalance or vitiation of one of the three Sarira Doshas (physical elements, Vata, Pitta, Kapha); somaticized conditions; e.g., Aswapna (insomnia) and avasthita Chittatva (fickle mindedness)

**Nasya** -nasal instillation; one of the Cikitsa Sutra (treatment principles)

**Nidana**-etiology of a disease; causative factors; pathology

**Nidann Parivarjana**-identification and avoidance or elimination of the causative factors of a disease; essential for the successful management of both Sarira (physical) and Manasa Rogas (mental diseases)

**Nidra**-sleep

**Nija**-disease etiologies that are contributed by inherent or Intrinsic (endogenous) factors acquired after the stage of conception

**Nija Rogas** -a disease having an endogenous etiology due to irregular food habits and psychobehavioral excesses resulting in the impairment of the Sariradosha (physical elements); Charaka's classification of disease based on etiology

**Nindradhikya** - hypersomnia

**Niyama, Homa**-sacrifice, vows; used in Daivavya-pashraya Cikitsa (spiritual or divine therapy)

**Oleation**-oil treatment; internal oleation with Ghritas (medicated ghees prepared with herbs and animal products that are particularly good for tranquilizing the mind and cleansing) are used in Panchakarma (purification therapy)

**Ooha**-anticipation; guess

**Paisachika**- a Ghrita (medicated ghee) used as an internal oleation (oil treatment) In Panchakarma (purification therapy)

**Paisunya**-abusive or harsh speech

**Palitya**-premature graying

**Panasa**-jackfruit; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Pancagavya Ghrita**-a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Pancendriya Pariksa** -physical examination of-the patient; it consists of Astavidha Pariksa (general survey) by Nadi (pulse), Mutra (urine), Mala (stool), Jihwa (tongue), Sabda (voice), Spasa (sl-jn), Drk (eye), and Akriti (facial expression or appearance); and Sadanga Pariksa (systemic examination of the six parts of the body including the head-neck, trunk, and the four limbs along with the 13 Srotamsi (channels) distributed over

the Sadanga (body))

**Panchabhautik, Panchabhautika** -made up of the five basic physical factors or elements: Akasa (ether or space), Vayu (air or motion), Teja (fire or radiant energy), Jala (water or cohesive factor), and Prithvi (earth or mass)

**Panchakarma**-fivefold internal purification and cleansing therapy; it consists of Vamana (emesis), Virecana (purgation), Anuvasana Vasti (oleus enema), Asthapana (nonoleus enema), and Siro-virecana (nasal instillations); also known as Samshodhana Karma or Shodhana Karma; it usually follows external purification - oleation, fomentation, and massage; it is a preparatory for Samsamana (curative treatment)

**Pancha Mahabhutas**- the five basic physical factors or elements making up the mind, body, and universe

**Pariksa** - examination

**Parinama**-seasonal variations; chronobio-logical changes occurring in the body as a result of alterations in time factors such as diurnal variations; an important factor in the causation of physical and mental disease

**Paryusita**- stale food

**Pitta**- bile; one of the three Sariradoshas (physical elements)

**Pitta Prakriti**-the Prakriti (personality) type dominated by Pitta-prone to excitation but strong

**Pizhichil**- irrigation of the body with oils, squeezing clothes wet with oil and allowing this oil to fall on the body and smearing with light massages; purification treatments used at Kerala

**Prajnaparadha** -deliberate or volitional transgression or misuse of body, mind, and speech; an important factor in the causation of physical and mental disease

**Prakopa**-one of the six stages in the evolution of disease; the stage of vitiation of the Doshas

**Prakriti, Prakritis** - personality or constitution; part of the tenfold Rogi Pariksa (examination of the patient) to ascertain the individuals state of health; personality disorders resulting from an overt imbalance in Manas Prakritis (mental traits) accompanied by abnormal behavior

**Pramada**-inimature or weak character; infatuation; delusion

**Pramana**-observations, measurements; anthropometry; part of the tenfold Rogi Pariksa (examination of the patient) to ascertain the individual's state of health; the three fundamental ways of knowing or measuring including direct perception, inference, and textual testimony



- Pranavahasrota**- respiratory tract
- Pranayama** -a method for achieving Manoni-graha (mental control) by the use of Abyasa (intense study) and Vairagya (renunciation)
- Pranipata, Prayascita**-penitence and prostrations; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)
- Prasanna**-a state of sensorial, mental, emotional, and spiritual well-being; one of the characteristics of a Swastha (healthy person)
- Prasara**-one of the six stages in the evolution of disease; the stage in which the disease spreads
- Prasna Pariksha**-interrogation of the patient and/or a reliable informer; patient history; part of the clinical examination of the patient
- Pratyahara**-a type of Manonigraha (mental control) in which the mind is withdrawn from sensory functions
- Pratyaksa** -direct perception
- Prayascita, Pranipata**-penitence and prostrations; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)
- Prithvi**- earth or mass; one of the Pancha Mahabhutas-five essential elements of matter-, the Pancha Mahabhutas are represented in the psyche of an individual in terms of the Manas Gunas (qualities of the mind, mental constitution)
- Puman, Cetana**-the unification of Satva (mind), Atma (spirit, soul), and Sarira (body) in a human being
- Punarjanma**-rebirth
- Pundit**- a learned person
- Purusa**-individual
- Purvarupa** - prodromal features of a disease which appear during the onset
- Raga**-infatuation
- Rahaskamata**-fond of solitude, remaining secluded, secretive about desires and activities; a symptom of Kaphajonmada
- Raja, Rajas**-passion; one of the Manasa Doshas (elemental substances of the mind)
- Rajas Prakriti**-the Rajas personality; one of the three broad categories of Prakritis (personalities); the Prakritis are further divided into 16 Manas Prakritis (mental traits) which predispose an individual to a specific disease
- Raksas**-an evil spirit
- Rakta**-blood
- Rasa**-plasma and lymph; taste
- Rasayana**-rejuvenators or tonics; Rasayana plants or drugs are used to promote health, prevent disease and aging
- Rasayann Tantra**-nutrition, rejuvenation, and geriatrics, one of the eight major specialties of Ayur-vedic medicine
- Ratricarya** - health conduct for the night; it is part of Swastha Vritta, a comprehensive regimen for maintaining health
- Ritucarya**-health conduct in relation to various seasons; it is part of Swastha Vritta, a comprehensive regimen for maintaining health
- Roga**-imbalanced state of the Doshas (elemental substances of the mind and/or body); disease
- Roga Pariksha**- examination of the disease pathology; the exam is done in three parts-patient history, eightfold general exam, and systemic exam of the Srotamsi (13 gross channels of the body) including pulse reading
- Rogi Pariksha** -examination of the patient to ascertain the constitution and evaluate the status of health and vitality; it consists of a tenfold exam of Prakriti (constitution), Vikriti (disease susceptibility), Sara (quality of the tissues), Samhanan (compactness of the body), Pramana (anthropometry), Satmya (adaptability), Satva (mental stamina), Ahara Sakti (digestive power), Vyayama Sakti (physical strength), and Vaya (age and rate of aging)
- Rupa** -clinical profile or features of a disease which appear when the disease is fully manifested
- Sabda**-voice, sound
- Sadanga, Sadangas**-the six major parts of the body including the head-neck, trunk (chest, abdomen) and extremities; it is assessed in the Sadanga Pariksha (physical examination of the body)
- Sadanga Pariksha**-systemic examination of the 6 parts of the body including the head-neck, trunk, and the 4 limbs along with the 13 Srotamsi (channels) distributed over the Sadanga(body)
- Sadhyasadhyata, Sadhyasadhyatva** -prognosis
- Sadvritta**-code or virtues; e.g., lifestyle, diet, exercise, and personal and social hygiene; good acts
- Sahaja**-disease etiologies that are contributed by inherent or intrinsic factors acquired at conception
- Salakya Tantra**-diseases of eye, ear, nose, and throat, one of the eight major specialties of Ayurvedic medicine
- Salya Tantra**- surgery, one of the eight major specialties of Ayurvedic medicine
- Sama**-balance
- Samadhatu Prakriti**-the Prakriti (personality) type in which all of the Doshas (physical elements -Vata, Pitta, Kapha) are equal; it is



considered to be the best personality

**Samadhi**-concentration; the state attained by Yogic meditation

**Samana, Samsamana**-curative therapy; it is based on an individual's Prakriti (constitution) and Vikriti (disease susceptibility)-pattern of vitiation of the Doshas (physical elements), Dhatus (bodily tissue groups), and Agni (digestion and metabolism); it includes rationally planned use of drugs through oral route, and nondrug therapeutics such as fasting, diet, and lifestyle; it is used following Samsodhana Karma (purification therapy; Panchakarma)

**Samanya and Visesa**- the concept of homologous and heterologous; similar or homologous matter increases itself, whereas dissimilar or heterologous matter decreases or depletes itself-, this principle is used to formulate the specific Samsamana (curative treatment consisting of diet, drugs, and lifestyle) to restore homeostasis

**Samayoga**-process of unification

**Sambhinnalepa**-incongruous talking

**Samhana**-body build, compactness of the body; part of the tenfold Rogi Pariksha (examination of the patient) to ascertain the individual's state of health

**Samkhapushpi**-Clitoria ternatea; an herb used in Rasayanas (tonics) for purification in longstanding diseases

**Samprapti**-pathogenesis of a disease, consisting of an interaction between the Doshas and Dusyas (local tissues)

**Samsodhana Karma**-purification and cleansing therapy; also known as Panchakarma or Shodhana Karma; external purification uses oleation, fomentation, and massage to soften and mobilize the Malas (impurities); it is followed by internal purification-Vamana (emesis), Virecana (purgation), Anuvasana Vasti (oleus enema), Asthapana (nonoleus enema), and Sirovirecana (nasal instillations); it is followed by Samsamana (curative treatment)

**Sancaya**-the beginning stage in the evolution of disease; the stage of accumulation of the Doshas

**Sandhya**-a Vedic ritual performed at dawn and dusk

**Sanghatbala Pravritta**-traumatic; classification of disease based on presumed causative factors Sanjnajnana-orientation and responsiveness Sannipata Unmada -a type of Nija Unmada (severe endogenous mental disorder); its signs, symptoms, and psychopathology are due to an imbalance in all three Doshas (elements); this type has the most severe

prognosis

**Santarjanam**-threatening; a symptom of Pittajonmada

**Santvana**-consolation

**Sanyasa** - syncope

**Sara** -quality of the tissues; part of the tenfold Rogi Pariksha (examination of the patient) to ascertain the individual's state of health

**Saraswata Curna**-a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Saraswatarista**-a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Sarira**-body, physical

**Sariradhisthana**-body-based disease; an example Is Jwara (fever)

**Sariradosha, Sariradoshas**-the physical elements or Doshas of the body: Vata (wind), Pitta (bile), and Kapha (phlegm); the physiological constitution of a person is based on the balance of these three Doshas; an imbalance in the Sariradoshas can result in physical disease

**Sariraja**-physical; diseases are classified as Sariraja if there is a predominance of physical elements (Dosha)

**Sariramanoadhisthita Manovikara (SMMV)**-body mind-based Manovikara (mental disorders), the somatopsychic disorders; one of two subtypes of Ubhayadhisthita (dual type) Manovikara (UMV); e.g., Unmada (psychosis), Apasmara (epilepsy)

**Sarirashraya**-body-dependent disease, classified according to its Adhisthana (seat of origin); e.g., Kushtha (dermatitis), Atisara (diarrhea)

**Sariravikara**-physical illness

**Saririka Doshas**-the physical elements of the body, Vata (wind), Pitta (bile), and Kapha (phlegm); the Tridoshas

**Sarpa Mamsa**-snake meat; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Sarpagandha**-a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Satavari**-Asparagus racemosus; a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Satavari Leha**-a Rasayana (tonic) used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Satkriyakala**-six stages in the evolution of a disease

**Satmya**-adaptability; part of the tenfold Rogi Pariksha (examination of the patient) to ascertain the individuals state of health

**Satva**-pure consciousness; clarity; mental stamina; absolute balance of the extreme qualities of mind, Rajas (passion) and Tamas (inertia); part of the tenfold Rogi Pariksha (examination of the patient) to ascertain the



individual's state of health

**Satvavajaya**-the method of restraining the mind from Arthas (unwholesome objects)

**Satvavajaya Cikitsa**-psychobehavioral therapy used in the management and treatment of a psychiatric patient; it incorporates the principles of Asvasana (assurance therapy), replacement of emotions, and psychoshock therapy

**Satvika Prakriti**- the Satva personality; one of the three broad categories of Prakritis (personalities); the Prakritis are further divided into 16 Manas Prakritis (mental traits) which predispose an individual to a specific disease

**Shalya Cikitsa** -surgery

**Shastrasadhya**- surgically treatable disease

**Sheegra Sambraham**-eager to start but neither sustain nor complete an activity; a symptom of Vatajonmada

**Shelshmoda Gharnacha**-bronchial hypersecretion

**Shodhana Karma**-purification and cleansing therapy; also known as Panchakarma or Karma; external purification uses oleation, fomentation, and massage to soften and mobilize the Malas (impurities); it is followed by internal purification-Vamana (emesis), Virecana (purgation), Anuvasana Vasti (oleus enema), Asthapana (nonoleus enema), and Sirovirecana (nasal instillations); it is followed by Samsamana (curative treatment)

**Shoka**-sadness, grief

**Shokaja**-grief-induced

**Shokajashosha**-grief-induced emaciation

**Shouchadwesa**-hatred towards cleanliness, lack of hygiene, poor personnel care; a symptom of Kaphajonmada

**Shukra**-male reproductive tissues

**Siddha**-those who have accomplished spiritual perfection

**Sila**-habits or temperament, including personal care, affective behavior, biological functions, and physiological functions

**Sira**-veins

**Siro Lepa**-application of wet cakes on the head and on the Vertex; one of the Cikitsa Sutra (treatment principles)

**Smriti**-memory

**Smriti Sagar Rasa**- a compound used in Yuktivyapashraya Cikitsa (diet-drug therapy)

**Smritisagar Rasa**- an Ayurvedic formulation used for the treatment of epilepsy

**Snehadisadhya**- medically treatable disease

**Soka**-sorrow, grief-, one of the Manas Dosha Vikaras caused by excessive Soka

**Sokaja Unmada**-mental anguish due to stress, loss, or shock

**Sokatisara**-diarrhea of psychological origin; an example of a Manodaihika Vyadhis (psychosomatic disease in which the cause is mental and the manifestation is somatic)

**Solanum nigrum** - Solanum nigrum, Kakamaci; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)

**Sparsa**-touch

**Srotamsi**-thirteen gross channels of the body

**Srotas** -channels or pathways of the mind or body; blockade of the Srotas can trigger Sancaya (accumulation of Doshas), the first stage in the evolution of a disease

**Srotas Pariksa**-physical examination of the Srotas or Srotamsi (channels) of the body; in a psychiatric examination, Srotas Pariksa includes examination of the Manovaha Srotas (channels of the mind or state of mind)

**Sroto Dusti**-vitiation of the sense of touch

**Stanyanasha**-loss of lactation

**Steja** - stealing

**Sthana Samsraya**-one of the six stages in the evolution of disease; the stage in which the disease becomes localized

**Sthanamekadeshe**-confinement to one place or posture; a symptom of Kaphajonmada

**Stymityam Shetangiche** -sweating

**Supta-Unmatta-Pramatta** - confused

**Sutra**-principles

**Swabhabala Pravritta**-natural or inherent; classification of disease based on presumed causative factors

**Swabhavika** -natural, refers to the classification of disease according to causation

**Swabhavoparamvada** - self-healing; natural-selfcure

**Swanigraha**-mental control; self-control

**Swastha** - a healthy person who is in a state of total biological equilibrium as well as Prasanna (a state of sensorial, mental, emotional, and spiritual well-being)

**Swastha Vritta** - a comprehensive regimen for maintaining health based on daily and seasonal routines; it includes Dinacarya (the daily code of health conduct), Ratricarya (conduct for the night), and Ritucarya (conduct in relation to various seasons)

**Swasthya**-the four-dimensional concept of health defined by Sushruta; a state of Sama (balance) of the 3 Doshas, the 13 Agnis (digestive or metabolic factors), the 7 Dhatus (bodily tissue groups), and the Malas (impurities)

**Swatamutracha**- involuntary micturition

**Tadana**-whipping



- Tagara**-a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)
- Tailadhara**-decoctions of herbals; one of the Cikitsa Sutra (treatment principles)
- Takradhara**-streaming of medication; one of the cikitsa Sutra (treatment principles)
- Talam**-applying oils or medicine on the head in the form of a circle; purification treatments used at Kerala
- Tama, Tamas** -inertia, lethargy; one of the Manasa Doshas (elemental substances of the mind)
- Tamas prakriti** -the Tamas personality, one of the 3 broad categories of Prakritis (personalities); the Prakritis are further divided into 16 Manas Prakritis (mental traits) which predispose an individual to a specific disease
- Tandra**-Drowsiness, stupor; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the sarira (physical-Vata, pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas
- Tarjana**-verbal threatening
- Teja** - fire or radiant energy; one of the Panch Mahabhutas-five essential element of matter; the Panch Mahabhutas are represented in the psyche of an individual in term of the Manas Gunas (qualities of the mind, mental constitution)
- Thriphala**-Three myrobalans; an herb used in Rasayanas (tonics) for purification in longstanding diseases
- Trasana**-frightening
- Tridoshas**- the three physical elements or Doshas: Vata (wind), Pitta (bile), Kapha (phlegm); the physiological constitution of a person is based on a balance of the Tridoshas
- Tridosika arrhythmia**-vitiation or one or more of the three Doshas (physical elements); may lead to irreversible diathesis and evolution of disease
- Trigunas** -the three Gunas (qualities) of the Manas (mind): Satva (clarity), Rajas (passion), and Tamas (inertia); the Pancha Mahabhutas (five basic elements) are represented in the psyche of an individual in terms of the Gunas
- Triptisha**-nausea
- Ubhayadhisthita Mauovikara (uMV)**-dual type (mind- and body-based) Manovikara (mental disorders); one of two major types Of Manovikaras
- Ubhayasrita Manasikaroga** - one of the two types of Manasaroga (imbalanced state of mind or Manas) as classified by Achal 1976; dual type (mind- and body-based); e.g., Anidra (insomnia, sleeplessness), Madatyaya (alcoholism), Unmada (psychosis)
- Ubhayatmaka**-dual type diseases; conditions with a predominance of both Manasa (mental) and Sariraja (physical) Doshas (elements)
- Ubhayadhisthana**-conditions with a dual type, (mind- and body-based) seat of origin; e.g., Unmada (psychosis)
- Udvega**-neurosis; one of the Manas Dosha Vikaras caused by excessive Udvega
- Unmada**- psychosis, severe mental disorder; a psychiatric condition caused by mixed Samprapti (pathogenesis) including both the Sarira (physical-Vata, Pitta, Kapha) and Manas (mental-Rajas, Tamas) Doshas
- Unmada Gajakesari**-an Ayurvedic formulation used for the treatment of Unmada
- Unmada Roga**-psychotic diseases, e.g., Agantuja Unmada or Bhutonmada
- Upakara, Bali**-oblations or offerings; used in Daivavyapashraya Cikitsa (spiritual or divine therapy)
- Upasaya**-drugs, diet, lifestyle
- Urdhang Cikitsa**-ear, nose, throat, and eye
- Vaca**-Acorus calamus; a drug used in Yuktivyapashraya Cikitsa (diet-drug therapy)
- Vaidya**-physician, healer
- Vairaga** - renunciations
- Vak Vikarah**-irrelevant, incoherent, excessive speech; a symptom of Vatajonmada
- Vastuka**-Chenopodium album; used in Yuktivyapashraya Cikitsa (biological or diet-drug therapy)
- Vata**-wind; one of the three Sariradoshas (physical elements)
- Vata Prakriti**-the Prakriti (personality) type dominated by Vata -weak, melancholic, with weak power for excitation and inhibition
- Vaya** -age and rate of aging; part of the tenfold Rogi Pariksa (examination of the patient) to ascertain the individual's state of health
- Vayu**-air or motion; one of the Pancha Mahabhutas-five essential elements of matter; the Pancha Mahabhutas are represented in the psyche of an individual in terms of the Manas Gunas (qualities of the mind, mental constitution)
- Vedas** -the four ancient books of Indian knowledge and wisdom, philosophical tradition, and spiritual practice: Rig, Sama, Yagur, and Atharva Vedas
- Vicara**-thought process
- Vihara**-lifestyle
- Viharajanya**-disease states in which habits are the causative factors
- Vijnana**-professional knowledge
- Vikalpa**-one of the five categories of Citta Vritti



- (fluctuations of the mind)
- Vikriti**-current state of disease susceptibility or morbidity
- Viparyaya** -one of the five categories of Citta Vritti (fluctuations of the mind)
- Virecana**-purgation; one of the Cikitsa Sutra (treatment principles)
- Viruddhahara**- incompatible food
- Virya** -potency of pharmacological action of matter or drugs
- Visaja Unmada**-mental anguish due to poison
- Visala**-Citullus colocynthis an herb used in Rasayanas (tonics) for purification in longstanding diseases
- Visamahara** -irregular food habit
- Vishada**-depression, lassitude
- Vishaja Unmada**-toxic psychosis
- Vishayakara** -fluctuations of the mind-, Citta Vritti
- Vismaya** -showing wonders
- Vismriti**-diversion, distraction
- Vitiati**-imbalance in the Doshas (physical or mental elements); may lead to irreversible diathesis and evolution of disease
- Vrasha Cikitsa**- endocrinology and the reproductive system
- Vrhatrayi**-three bigbooks,Caraka Samhita, Sushruta Samhita, and the Samhitas of Vagbhatta; an ancient Ayurvedic text originating from the Vedas
- Vrida** -elderly people
- Vritta**-codes
- Vyadhi**-people who are suffering from disease
- Vyadhi Bala**-strength of the disease
- Vyadhiksamatva**- natural resistance and immunity of the body against disease
- Vyakti**-one of the six stages in the evolution of disease; the stage in which the disease becomes manifest
- Vyapada**-quarreling, intention of harming
- Vyayama Sakti** -physical strength; part of the tenfold Rogi Pariksa (examination of the patient) to ascertain the individual's state of health
- Yoga**-a state of Citta Vritti Nirodha (controlled mind); discipline for attaining a higher state of consciousness through intense concentration, meditation, prescribed postures, controlled breathing, etc.; Yoga practices are used in Satvavajaya Cikitsa (psychotherapy)
- Yukti**-experimental evidence
- Yuktivijnana**-rational knowledge
- Yuktivyapashraya Cikitsa**-diet- drug, rational, or biological therapy used in the management and treatment of psychiatric patients; it consists of Samshodhana Karma (purification therapy or Panchakarma) and















